BINOCULAR VERSUS MONOCULAR VIEWING

IN AGE RELATED MACULAR DEGENERATION

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Above all and beyond all,
this thesis is dedicated to my husband, Thanos,
the inspiration of my whole life...

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ABSTRACT

Purpose: This thesis compares monocular versus binocular viewing in AMD patients during fixation and reading, the potential of binocular function and the impact of symmetry of central scotomas on these results.

Methods: Thirty patients with bilateral AMD were recruited. Standard clinical tests (distance and near acuity, contrast sensitivity, stereoacuity) were performed monocularly and binocularly. Fusion at the fixation locus was tested with a computer-driven display using shutter glasses. A scanning laser ophthalmoscope was used to map the preferred retinal locus (PRL) and the retinal scotomas under monocular viewing conditions during a fixation task. An infra-red eyetracker was used to investigate gaze position changes (and indirectly retinal locus changes) during monocular versus binocular fixation of the same target. Data from both devices were combined to predict PRL position under binocular viewing. Reading speed and eye movements during reading were measured monocularly and binocularly using the eyetracker.

Results: Only 17.3% of AMD patients used the same PRL to fixate in both eyes under monocular versus binocular conditions, of whom 44.5% had symmetrical scotomas and 22.3% had asymmetrical scotomas. Retinal correspondence of the PRLs was retained in 85.2% of patients. Fusion at the PRL was demonstrated for most patients with symmetrical scotomas but for the minority of patients with asymmetrical scotomas (71.4% versus 33.3%). Reading speed binocularly could be accurately predicted by the reading speed of the better eye. There was no difference in eye movements during reading between the two viewing conditions.

Conclusions: Overall, there was little advantage in binocular versus monocular viewing. Patients demonstrated different PRL characteristics under these conditions and the symmetry of the retinal scotomas was the main factor to account for these differences. These results provide an insight into how people with bilateral scotomas operate in the real world. This information is essential for developing effective vision rehabilitation.

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INTRODUCTION

Age- related maculopathy (ARM) is a progressive degenerative disorder of the macula, which in its early stage among whites, affects 15% of patients aged 65-74 years, 25% of patients aged 75-84 years and 30% of patients over 85 years (Holz et al. 2003). It is the leading cause of legal blindness in the Western nations as late stage manifestations of the disease (late ARM or age related macular degeneration- AMD) usually have poor visual prognosis for most of the patients. Visual impairment in AMD is the result of the development of a blind spot or scotoma in the most sensitive central area of the field of view, the fovea. In order to accomplish visual tasks such as fixation, reading or recognising faces many patients adopt a peripheral non- foveal retinal locus that acts as a pseudo-fovea.

AMD often affects the two eyes differently regarding the size and the location of the scotomas. This binocular incongruity may interfere with the development of eccentric viewing (non-foveal fixation), normal eye movement co-ordination and binocular function. In that respect, eye movements cannot be studied accurately by studying each eye separately; the retinal locus used for fixation in one eye does not necessarily correspond with the retinal locus in the other eye and it cannot be predicted which retinal locus will be used if the subject uses both eyes.

The purpose of this study is to investigate the impact of similar and dissimilar scotomas on the development and stability of eccentric viewing and the potential binocular function in patients with bilateral AMD. The impact of these factors on the performance of visual tasks such as reading will also be evaluated. The results of this study will aid our understanding of patients' monocular versus binocular visual behaviour. They will also provide a useful insight into how people with bilateral scotomas operate in the real world. This information is essential for developing effective vision rehabilitation.

CHAPTER 1

AGE-RELATED MACULOPATHY

The overall prevalence of late age related maculopathy (AMD) in patients aged 65-74 years is 1%, 75-84 years 5%, and 85 years and over, 13% (Holz et al. 2003). AMD is the leading cause of blindness in the developed world (Robinson et al. 1997) and is responsible for approximately 50% of all blind and partially – sighted registrations in England and Wales (Evans et al. 1996). Although age is a significant risk factor for ARM (Klein et al. 1991), recent analysis indicated that the prevalence of the disease seemed to be increasing at a faster rate that was expected by the increasing age of the population (Evans and Wormald 1996).

1.1. AETIOLOGY AND PATHOGENESIS

The aetiology of ARM is poorly understood but it is thought that it is a multifactorial disease. ARM presents with an intraindividual symmetry in the presence of a wide range of interindividual variability (Bellmann et al. 2002). This suggests heterogeneity at a cellular and molecular level, which is not merely the result of a non-specific ageing process in ARM. Twin studies support a multi-factorial disease but assume a primarily polygenic aetiology for ARM (Hammond et al. 2002; Grizzard et al. 2003).

Risk factors

The main predisposing factor for ARM is age. Other significant risk factors include ocular risk factors (soft drusen, macular pigmentary changes and choroidal neovascularisation in the other eye) and systemic risk factors (positive family history and tobacco smoking).

Other factors reported to be associated with an altered risk of ARM include demographic factors (female sex, level of pigmentation), cardiovascular factors (such as hypertension and atherosclerosis), light exposure, environment and nutrition (Age-Related Eye Disease Study Research Group 2000; Evans 2001;

Smith 2001). However, the data seem to be inconclusive with respect to the exact role of the latter factors.

Pathogenesis

ARM is thought to be a complex disease affecting photoreceptors and retinal pigment epithelium (RPE) as well as underlying Bruch's membrane and choriocapillaries. The locus of the primary insult remains unclear. Impaired phagocytosis of photoreceptor outer segments by RPE results in lipofuscin accumulation. Lipofuscin is a group of autofluorescent lipid and protein aggregates. With advancing age, lipofuscin accumulation in the RPE increases and it is concentrated in the macula. It forms amorphous deposits lying between the basement membrane of the RPE and Bruch's membrane termed as drusen. Lipofuscin accumulation produces a hydrophobic barrier in Bruch's membrane (Curcio 1999) and can also potentiate phototoxicity, which affects its normal function. Degeneration and atrophy of the RPE cells eventually occurs. Moreover, haemodynamic changes resulting in impaired choroidal blood flow have been implicated in ARM pathogenesis, together with angiogenesis and inflammation models. In this multifactorial hypothesis apoptotic cell death involves photoreceptor death and degeneration or atrophy of the choriocapillaries.

1.2. CLINICAL PRESENTATION

ARM mainly affects the central part of the retina (macula). This is the region with highest photoreceptor density and therefore responsible for fine spatial vision. There is a variety of clinical presentations of ARM. The International ARM Epidemiological Study Group attempted to classify Age Related Maculopathy (ARM) and AMD in 1995 (Bird et al. 1995). Early ARM is defined as the presence of drusen and retinal pigment epithelium (RPE) pigmentary abnormalities (hypopigmentation and hyperpigmentation). Late ARM is similar to age related macular degeneration (AMD) and it can present as geographic atrophy (loss of photoreceptors and retinal pigment epithelium), or neovascular AMD including detachment of the retinal pigment epithelium, choroidal neovascularisation and disciform scars.

Clinical symptoms depend on the type of ARM. Quite frequently it is only when visual loss occurs in the 2nd eye that symptoms arise. The presence of drusen alone may not give rise to symptoms and visual acuity may be normal. Distortion and/or decrease in visual acuity are common symptoms of choroidal neovascularisation. Further decrease in visual acuity occurs either as a result of blood from the choroidal neovascular membrane leaking into the tissues, scarring or geographic atrophy. These changes can lead to irreversible degeneration of the neurosensory retina (Bressler et al. 1990) with a dismal visual prognosis for most of the patients with AMD. Due to the loss of photoreceptor function, AMD patients develop a scotoma in the central visual field that is mainly responsible for their visual impairment. Hence, many important daily vision tasks such as reading, and face recognition are compromised (Timberlake et al 1986; Whittaker et al. 1988).

Symmetry and asymmetry of macular lesion in ARM

Bilateral eye involvement in ARM has long been recognised, and the frequency of second eye involvement has been documented in a number of retrospective and prospective case series (Gregor et al. 1977; Strahlman et al. 1983; Roy and Kaiser Kupfer 1990; Bressler et al. 1990; Macular Photocoagulation Study Group 1993a). Nevertheless, both eyes are not affected simultaneously so most of the patients experience some degree of asymmetry in macular lesions during the course of the disease. However, as the major determinant of ARM is age (Klein 1992; Sperduto 1980; Vingerling 1995) it is expected that bilateral involvement will increase with age.

Geographic atrophy (GA) has been estimated to occur bilaterally in 48% to 65% of the cases (Potter 1981; Sarks et al.1988; Green et al. 1985). Sunness and coworkers (Sunness et al. 1999) described a high correlation in the size and progression of GA between both eyes. Several previous studies (Sunness et al. 1999, Maguire and Vine 1986, Schatz 1989) have described the progression of GA over time.

In general, GA usually commences within a parafoveal band of atrophy of varying width. Progression of atrophy mostly skirts fixation and visual acuity is a poor guide to the functional impact; an estimate of the percentage of fovea

involved proving a more useful clinical parameter (Sarks et al. 1988). The rate of progression slows once GA has involved all the macula affected by incipient atrophy. A prospective study on the natural history of the progression of GA by Sunness (Sunness et al. 1999) demonstrated a mean enlargement of the total area of GA of 2.2 disc areas by 2 years. They reported that the amount of enlargement increased with increasing baseline total atrophy up to 5 disc areas of baseline atrophy and leveled off when it reached above 5 disc areas. Bellmann and coworkers (Bellmann et al. 2002) also reached similar conclusions using a scanning laser ophthalmoscope to evaluate and measure retinal lesions.

Symmetry of retinal lesions due to ARM has also been evaluated for drusen, CNV, and RPE tears (Barondes et al. 1990; Chuang and Bird 1988; Wang et al.1998). All groups concluded that there were high rates of symmetric manifestations of ARM between the two eyes. A study of the symmetry of disciform scars (Lavin et al. 1991) also found a significant correlation between eyes in terms of the final scar size, and it was predicted that large macular scars were more frequent in the second eye if the first eye had a large scar.

In general, the conclusions of these studies described symmetry of macular lesions due to ARM. Nevertheless their results were based on simply calculating the overall number and size of retinal lesions (single or multiple retinal lesions) for each eye. There were no measurements to describe the location and distribution of these lesions with respect to the normal fovea for both eyes. Therefore, no real reports of the congruity or incongruity of the macular lesions between the two eyes have been provided. Their findings support the view that genetics may play an important role in the phenotypic appearance of ARM but they don't provide any information on how bilateral lesions can affect patients' binocular behaviour.

1.3. MANAGEMENT

The management of AMD should be threefold. Prevention modalities and treatment options should be combined with rehabilitation strategies in order to deal with AMD patients in a holistic way.

1.3.1. Prevention - Prophylactic modalities and treatment

Observational and experimental studies have suggested that antioxidants and/or zinc supplements can delay the progression of AMD. In a large clinical trial, high doses of vitamin C, E, beta-carotene and zinc (recommended dose: vitamin C 500mg, vitamin E 400 IU, beta-carotene 15mg, zinc oxide 80 mg , and Copper 2 mg) showed a significant benefit in certain groups of AMD patients. In particular in this study, AMD patients with extensive intermediate size drusen, at least one large drusen, non-central geographic atrophy or advanced AMD in one eye (AREDS 2001) showed a significant benefit in protecting against progression to advanced AMD of about 25%. Therefore, patients with intermediate AMD and without contraindications should consider using antioxidant plus zinc supplements. However, there is no evidence to date to suggest that earlier use conveys benefit.

The antioxidative and blue-light filtering effects of lutein and zeaxanthin found in macular pigment are considered to be most effective against light damage. Ageing causes a reduction in these pigments (Hammond and Caruso-Avery 2000) and this could be a risk factor for ARM (Beatty et al. 2001). As these pigments cannot be made by the body, their concentration depends on the diet and supplement intake, which can increase macular pigment and possibly play a role in the prevention of ARM (Holz et al. 2003). The use of supplementation with lutein for ARM prevention was investigated by the Lutein Antioxidant Supplementation Trial (LAST, which) was conducted to determine whether nutritional supplementation with lutein or lutein together with antioxidants, vitamins, and minerals, could improve visual function and symptoms in atrophic AMD (Richer et al. 2002; Richer et al. 2004). Although it was concluded that visual function was improved with lutein alone or lutein together with other nutrients further studies are needed with more patients, of both genders, and for longer periods of time to assess long-term effects of the treatment of atrophic age-related macular degeneration.

The observation that laser photocoagulation can alter the appearance and in some cases bring about resolution of drusen has led to a series of clinical trials for prophylactic argon laser therapy, even though the underlying mechanisms

are not fully understood. Most investigators have found a significant reduction of drusen after a relatively small number (12-100) of treatment burns (The Choroidal Neovascularisation Prevention Trial Research Group 1998a; Owens et al. 1999). However, the results of final visual outcome and the rate of CNV formation do not seem to be consistent in different trials. The overall results are not promising, as prospective trials have not reported an effect in 3 year follow up. In addition, early CNV formation has been reported in the treated group (The Choroidal Neovascularisation Prevention Trial Research Group 1998b; Owens et al. 1999). Overall, the results from the trials performed permit neither preliminary estimation nor final evaluation of long-term results (Holz et al. 2003) and prophylactic argon laser treatment of drusen in many clinical trials is still inconclusive.

1.3.2. Treatment

Treatment of AMD with conventional and novel techniques is of limited benefit to the majority of AMD cases (Chong and Bird 1998). No treatment is available for the atrophic form and current treatment possibilities for CNV aim mainly to stabilize visual acuity. Vascular ingrowth in exudative AMD causes remarkable physiologic alteration in the macular region, which can be detected by fluorescence angiography. The angiographic appearance of the CNV allows determination of its location (i.e. subfoveal- involving the centre of the foveal avascular zone, juxtafoveal- within 200μm from the centre of the foveal avascular zone but not involving it, extrafoveal- more than 200μm from the centre of the foveal avascular zone) and the type of the CNV (i.e.'classic' CNV and 'occult' CNV) that is important for the evaluation of the patient's suitability for treatment. In the fluorescein angiogram the 'classic' CNV is characterised by being easily visible in the early phase directly after dye injection, whereas in the mid- and late-phase, vessels are often obscured by the overlying fluorescein that has leaked from the vessels. The early hyperfluorescence in 'classic' CNV can appear as a brush or a cartwheel, whereas in 'occult' CNV the boundaries of the CNV are poorly demarcated and these changes may be only visible in the late phase.

Laser photocoagulation

One established treatment for AMD is focal argon laser photocoagulation of the CNV, as it was established by the Macular Photocoagulation Study Group (MPS) (Macula Photocoagulation Study Group. 1991a; Macula Photocoagulation Study Group. 1991b; Macula Photocoagulation Study Group. 1993b). However, less than 10% of AMD patients with CNV are suitable candidates for argon laser photocoagulation according to the MPS criteria, and in these patients the persistence or recurrence rate of the CNV is over 50% within 2 yrs. Moreover, recurrent CNV tends to be subfoveal. In 1991 the MPS group showed prevention of large decrease in visual acuity after 2 years follow-up and the benefits persisted for at least 4 years. Therefore, laser photocoagulation still remains the treatment of choice for classic juxtafoveal and extrafoveal CNV. Laser photocoagulation for subfoveal CNV is rather controversial. At 2 year follow up in the MPS study there was some benefit in patients with small membranes with poor visual acuities. However, laser photocoagulation destroys not only the CNV by coagulative necrosis but also causes collateral damage to the overlying retina. Thus, the sudden acquisition of a central scotoma and an immediate reduction in central vision occurs allowing little time for the patients to adjust.

Photodynamic therapy (PDT)

Photodynamic therapy combines the intravenous infusion of a photosensitive dye followed by light irradiation of the target tissue. A non-thermal laser is used with a specific wavelength (689nm), which corresponds to one of the absorption peaks of the dye (Schmidt-Erfurth et al. 1994). There is a preferential concentration of the photosensitizer in the target tissue (CNV) and thus the resulting photochemical reaction caused by the generation of reactive oxygen species causes local tissue damage without destroying the overlying retina. Therefore, a more selective treatment of the CNV is achieved.

Two identical multicentre, randomised, double-masked trials in Europe and North America using a photosensitizer called verteporfin have showed that PDT safely reduces the risk of visual loss in patients with subfoveal CNV. Specifically, the Treatment of Age-related Macular Degeneration with Photodynamic Therapy (TAP) Study started in 1996 and showed that PDT was of benefit in eyes with predominantly classic membranes (classic component

≥50%) and it approximately halves the risk of losing 15 letters of visual acuity at 2 years (59% versus 31%), with purely classic lesions performing best (53% versus 38%) ((TAP) Study Group. 1999; (TAP) Study Group 2001)). Therefore the TAP Study Group recommended PDT in the treatment of classic and predominantly classic subfoveal CNV. This means that as many as 20-30% of new AMD cases may be eligible for PDT on the basis of the TAP study (Bressler 2000).

Another large randomised controlled trial was initiated in 1998 to determine the efficacy of PDT for purely occult membranes (the Verteporfin in Photodynamic Therapy Study –VIP study) and eyes with early onset classic CNV with good visual acuity. The VIP Study Group found that PDT was efficacious in preventing vision loss in purely occult CNV (45% versus 32%) and although the overall benefit is small, it should be considered in the management of purely occult subfoveal CNV ((TAP) Study Group 2001).

In the U.K. the National Institute of Clinical Excellence published guidelines (September 2003) on the use of PDT. According to the current NICE guidelines PDT is recommended for AMD patients with 100% classic subfoveal CNV and best-corrected visual acuity between 6/12 and 6/60. PDT is recommended for the treatment of patients with predominantly classic subfoveal CNV (classic CNV ≥ 50%) only as part of ongoing or new clinical studies. A three-year UK-wide PDT Cohort Study has been set up to collect outcome data for PDT. The use of PDT in occult CNV was not considered because the photosensitising agent (verteporfin) was not licensed for this indication when this appraisal began.

In general, PDT can be easily performed on an outpatient basis as it is a minimally invasive technique, well tolerated by the patients and with a favourable safety profile. The main limitations of PDT are the need for multiple treatments (average of 5.6 in 2 years) ((TAP) Study Group 2001) and the high cost of the photosensitizers (Hooper and Guymer 2003).

The combination of PDT with other new techniques such as antiangiogenic substances, optimisation of treatment parameters or the use of new

photosensitizers are being explored in order to enhance the potential benefits of this treatment.

Transpupillary Thermal Therapy (TTT)

TTT is a laser technique which uses a long pulse near-infrared diode laser (810nm). It is mainly absorbed by the melanin of the RPE and choroidal melanocytes and transformed into heat (Berger 1997; Mainster and Reichel 2000). During treatment the temperature in the target issue increases to more than 45°C and therefore, below coagulation level. TTT was first used for the treatment of choroidal melanomas (Oosterhuis et al. 1995). Histologically, a thrombotic occlusion of the vessels within the treated tissue was demonstrated and this led to the use of TTT in neovascular AMD. The exact mechanism by which it closes CNV is unknown. Possible mechanisms that can also play a role are the thermal obliteration of vasculature and RPE migration, intravascular thrombosis, thermal inhibition of angiogenesis or neovascular apoptosis and heat shock proteins (Mainster and Reichel 2000; Ciulla et al. 2001; Desmettre et al. 2001). The first publication for AMD cases treated with TTT was by Reichel et al (Reichel et al. 1999). Since then, it has been used mainly in the treatment of occult CNV (Newsom et al. 2001). However, difficulties in calculating the exact power needed for effective treatment together with the incidence of irreversible visual loss with overtreatment are some of the problems with TTT (Holz et al. 2003). Overall, a therapeutic effect has been suggested, although, definite proof of its effectiveness has not been provided and routine application of TTT cannot be recommended. Current clinical trials are likely to answer these questions.

Surgical therapy

Surgical removal of the CNV

As the aforementioned treatment options are only limited to the minority of patients with AMD surgical alternatives have also been tried. Through a small retinotomy that allows transretinal access to the neovascular membrane, its surgical removal can be achieved (Hooper and Guymer 2003). Nevertheless, visual function remains poor not only due to the intraoperative risks and complications but mainly due to the accompanying damage to the surrounding retina and RPE (Gass 1994; Scheider et al. 1999).

Pigment epithelial cell transplantation

The above technique can be accompanied by pigment epithelial cell transplantation for better functional outcome (Scheider et al. 1999). The transplantation of homologous RPE, although it was successful in animal models, was not proven beneficial in humans due to the immunological rejection of the homologous or fetal RPE cells (Algvere et al. 1994; Algvere et al. 1997). To by-pass this response the use of autologous cells has been attempted (Majji and de Juan 2000), although this was a rather traumatic surgical procedure to obtain the cells. Moreover, the genetic predisposition of degeneration in the transplanted cells was still present and these could degenerate once transplanted to the subretinal space. The use of iris pigment epithelial cells instead of RPE that lack the predisposition for rejection and they can act as RPE in the subretinal space seem encouraging (Lappas et al. 2000; Thumann 2001). Employing genetically modified human RPE cell lines or transfected iris pigment epithelial cells is also being explored (Lund et al. 2001; Holz et al. 2003).

Macular translocation techniques

There is evidence that good central macular function can be gained if the fovea is translocated surgically over adjacent healthier RPE (Holz et al. 2003). The rationale behind this is that if visual function deteriorates as the photoreceptors remained over diseased tissue, by moving the fovea over a healthier area of RPE, Bruch's membrane and choriocapillaries, the photoreceptors can maintain or recover their function. This technique includes a 360° retinotomy with subsequent macular rotation (Machemer and Steinhorst 1993). Further modifications of this technique have also been proposed (Eckardt et al. 1999). A limited retinal rotation without a 360° rotation has also been explored (de Juan et al. 1998; Lewis et al. 1999).

Overall, of all surgical options available the latter (macular translocation techniques) seems a promising area that provides good distance and reading acuity. Prospective randomised trials are ongoing at present.

Radiotherapy

There is evidence that radiation therapy might be helpful in neovascular late stages of AMD, as there is a high susceptibility of proliferating endothelial cells of the new blood vessels to ionising radiation. In contrast, mature retina is relatively radioresistant. Two different techniques have been used for treatment; the teletherapy (external beam radiotherapy), which is the one most widely used, and the brachytherapy (episcleral radioactive plaques fixed surgically at the posterior pole of the eye) (Holz et al. 2003). A few studies showed some beneficial effect in patients with occult membranes compared with classic ones (Finger et al. 1996; Bergink et al. 1998) and in a large study the effect was significant in preventing visual loss (Valmaggia et al. 2002). The Radiation Therapy for Age-related Macular Degeneration (RAD) study group concluded that their results did not showed better functional outcome after treatment and trying different doses of treatment was thought to be unlikely to work (RAD Study Group. 1999). Therefore, definite evidence of the therapeutic effect of radiotherapy is still not current available, but it is a treatment that warrants further investigation (RAD Study Group. 1999; Hooper and Guymer 2003).

Pharmacological therapy

Pharmacological treatment using antiangiogenic drugs and angiostatic steroids (Challa et al. 1998; Pharmacological therapy for macular degeneration study group 1997; D'Amato et al. 1994; D'Amico, Slakter, Gillies et al., Eyetech Study Group) are currently trying to address the problem. Their aim is to block one or more pathways in the angiogenic process for the CNV development in exudative AMD. In particular, vascular endothelial growth factor (VEGF) can induce CNV formation and its blockage can inhibit the formation of CNV. Two clinical studies of VEGF inhibitors are under way –the Eyetech study (using a VEGF inhibitor known as pegaptanib) and the Genetech study (using an anti-VEGF antibody fragment; rhuFab). The results from phase III studies are pending.

Moreover, current randomised trials regarding the use of synthetic steroids, such as triamcinolone acetonide and anecortave acetate substances, are underway, investigating them as monotherapy or in combination with PDT.

1.3.3. Visual rehabilitation

While new strategies in the prevention and treatment of AMD will be developing during the next years, currently we have to deal with a rapidly increasing population which is visually disabled, and often socially isolated due to AMD. Therefore, visual rehabilitation plays an important role in the management of AMD patients.

1.3.3.1. Subjective complaints of patients with age related macular degeneration

Reading ability is disrupted in AMD patients and difficulty in reading is reported to be their most common complaint (Krieger 1967; Elliott et al. 1997; Hazel et al. 2000; Holz et al. 2003). Difficulty in reading newspapers and books were the main concerns of AMD patients followed by difficulty in reading mail and magazines (Wolffsohn and Cochrane 1999). In another study, reading 'ordinary print' was the major concern of AMD patients (Mangione et al. 1998). More details about the consequence of AMD on reading are presented in chapter 3.

AMD also severely impairs the ability of the patient to recognise faces (Bullimore et al. 1991) and this disability is one of the most common visual complains together with reading of AMD subjects (Mangione et al. 1999). Face recognition is an important factor of social interaction and it has been described as one of the most developed visual skills in humans. Face recognition impairment in AMD can be referred to failure to identify familiar faces or interpret facial expressions. More specifically, Bullimore and Bailey (Bullimore and Bailey 1991) found that for patients with poor face recognition performance, identity recognition was more severely affected than expression recognition, as the latter was considered to be less complex task to perform. Many face recognition tasks have been designed to assess AMD patients' visual performance. In most of the studies investigators attempted to quantify the level of visual impairment by relating these measurements to clinical tests of patients' visual function, such as distance visual acuity, reading acuity, contrast sensitivity or even colour vision (Bullimore and Bailey 1991; Tejeria et al. 2002). Tejeria et al. (Tejeria et al. 2002) suggested that distance visual acuity was related most closely to face recognition of familiar faces, while reading acuity was a better predictor of expression discrimination.

In general, it has been reported that patients with AMD were 8 times more likely to have difficulties when shopping, 13 more times more likely to have difficulty managing their finances, 4 more times more likely to have problems with meal preparation, 9 times more likely to report difficulty with light housework, and 12 times more likely to have trouble using a telephone compared with visually intact older people (Casten et al. 2004). These disabilities have a major impact on their personal and social life and their quality of life. Overall, the quality of life in AMD patients was reported to be substantially lower compared with normal-sighted older people, older people with severe chronic obstructive pulmonary disease, and patients with AIDS (Williams et al. 1998; Casten et al. 2004). Furthermore, AMD has a serious impact on psychological functioning that quite frequently can lead to depression. Several studies have reported the prevalence of depression among AMD patients as high as 33% (Brody et al. 2001; Rovner et al. 2002). Further research into this relationship revealed that the main cause of depression in AMD is the disengagement from enjoyable activities due to visual loss (Rovner and Casten 2002).

1.3.3.2. Vision rehabilitation strategies for AMD patients

Adaptation to visual loss involves developing strategies where residual vision can be best optimised. Visual rehabilitation is an adaptive process which involves the use of optical and non optical aids, development of viewing strategies and possibly the modification of the visual environment, including the use of new lighting and contrast enhancement techniques. It has been estimated that almost 60-80% of people with visual impairment have useful residual vision and benefit from visual rehabilitation in the long- term (Dickinson 1998).

A prerequisite in visual rehabilitation is to ensure that patients are given the optimal refractive correction. An additional step in visual rehabilitation is the provision of low vision devices. The use of magnifiers include optical devices such as plus lenses (spectacle- mounted, handheld and stand magnifiers) and telescopes, and electronic magnification devices such as closed circuit televisions (CCTV), which provide high magnification with a large field of view or head mounted TV systems that deliver bright images with high contrast

(Jordy, Maxport etc) (Margrain 2000). The non optical aids include sensory substitution such as taped reading (talking books and talking newspapers), kitchen aids etc (Dickinson 1998).

Optimization of lighting by increasing the general ambient light and enhancing illumination in a localised area to perform a detailed task is another important factor to improve performance of AMD patients. Moreover, environmental modification and building design are supplementary areas that rehabilitation services should be focused on (Dickinson 1998).

Social support for AMD patients can be provided by medical social workers based in hospitals (Culham et al. 2002) or local support groups. National charities such as the Royal National Institute for the Blind, the Guide Dogs for the Blind Association and the Macular Disease Society can provide further support to the visually impaired.

However, a recent National Eye Institute study found that very few older visually impaired patients were aware of the existence of low vision services and devices (Casten et al. 2004). Furthermore, as was earlier mentioned, AMD seems to be a disease whose effects extend well beyond visual disabilities. Depression is one of them. Thus, we need to be able to incorporate in our services the ability to identify those in need for further psychological support or even psychiatric treatment to aim for effective rehabilitation for AMD patients.

1.3.3.3. Aspects of PRL (preferred retinal locus) in AMD cases

As has already been mentioned visual loss in AMD is the result of the development of a blind spot or scotoma in the central area of the field of view, the fovea (Figure 1.1).

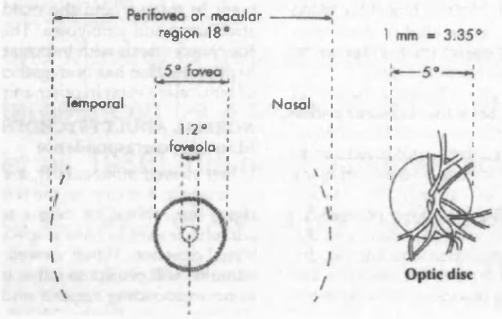


Figure 1.1. A schematic representation of the macular, foveal area and optic disc in a normal human retina (Adler's Physiology of the eye, 1992).

As a consequence of this reading, recognizing faces, or navigating independently becomes compromised. In order to accomplish these tasks many people with macular disease choose (consciously or unconsciously) a preferred eccentric area to perform the visual tasks that the non- functioning fovea used to perform (Schuchard and Fletcher 1994), which is called the preferred retinal locus (PRL). The concept of eccentric viewing was first defined by von Noorden in 1962 (von Noorden and Mackensen 1962) and is now well described in low vision research by many research groups.

Eccentric viewing naturally occurs when the foveal areas in both eyes are no longer functional due to 'absolute' central scotomas. Adaptation to macular scotomas under different conditions has already been reported (White and Bedell 1990; Guez et al. 1993; Schuchard 1995; Fletcher and Schuchard 1997; Lei and Schuchard 1997). The use of multiple PRLs has also been described in the literature (Whittaker et al. 1988; Lei and Schuchard 1997; Duret et al. 1999; Deruaz et al. 2002). Whittaker et al. reported that 39% of AMD patients demonstrated multiple PRLs (Whittaker et al. 1988). Interestingly, Crossland et al. presented data on patients using two or even three loci over a very short fixation trial experiment (Crossland et al. 2004a).

Many techniques have been employed to locate PRLs including fundus cameras (White and Bedell 1990; Nilsson et al. 1998), infrared eye trackers (Bullimore and Bailey 1995) or scleral search coils (Cummings et al. 1985). The most sophisticated instruments, mostly used in recent years, are the Scanning Laser Ophthalmoscopes (SLOs), which will be described in more detail later. Using the SLO a variety of fixation targets can be displayed including stationary and moving targets or even scrolled text (Culham et al. 1992). More specifically, targets can be a cross (Schuchard and Raasch 1992) or a square (Timberlake et al. 1986), diamond patterns (Schuchard and Raasch 1992), numbers (Guez et al. 1993) or letters (Timberlake et al. 1987; Culham et al. 1992) etc.

Many studies have also investigated the position of the PRL either with respect to visual field space or retina location. Most studies suggested that the PRL was placed below and left of the scotoma in visual space (White and Bedell 1990; Guez et al. 1993; Sunness et al. 1996; Fletcher and Schuchard 1997; Nilsson et al. 1998; Fletcher et al. 1999). Only the minority of patients seemed to place their PRL to the right or above the scotoma. It has been expected, especially for reading, that patients would place their PRL to the right of the scotoma as the visual span in reading English is 15 characters to the right of fixation and four to the left (Rayner 1975; Legge et al. 1997). The fact that more people preferred to place the PRL to the left of the scotoma instead of the right shows that people seems to read into rather than away from their scotomas. Although it has been proposed that this can be explained by the fact that 'monitoring', where fixation lands, depends mainly on the previous word, which is needed to be seen (Guez et al. 1993), no more reported data exist to support this hypothesis.

For unidentified reasons, eccentric viewing is not always automatically acquired in all cases of advanced bilateral AMD and even among those who use a peripheral retinal locus to fixate, we do not know how it is used during every day tasks such as reading and navigation. There is also a lot of debate as to whether patients are using the most optimal retinal location for their task (Culham et al. 1993) or if training towards this direction can improve their performance (Culham et al. 1997 ; Nilsson et al. 1998; Nilsson et al. 2003) (see below). Despite the conflicting views, it is generally believed that the development of appropriate eccentric viewing seems to be critical for effective rehabilitation, so it is important to identify the characteristics of the most useful PRL to aim for successful rehabilitation.

1.3.3.4. Improving visual behaviour in AMD

Pseudofoveation

White and Bedell in 1990 reported that over a period of years AMD patients with bilateral disease demonstrated a shift of the oculomotor reference system from the fovea to new non foveal locus used for fixation (White and Bedell 1990). Some patients demonstrated a complete re-referencing of their eye movements to the new preferred retinal area as they were able to maintain the target's image within a circumscribed retinal area during fixation using refixation

saccades. Patients believed that they were looking straight ahead when looking with their PRL. Furthermore in this study, some of the patients demonstrated complete absence of "foveating" saccades, as the image was projected directly on their PRL area without first projecting onto the area where the normal fovea used to be (within the scotomas). Schuchard et al (Schuchard 1995) also described that 8 out of 9 AMD patients in their study demonstrated no difference in their visual behaviour when they were asked to 'look straight at the target even if they were not able to see it clearly' or when they were asked to 'move their eyes so that the target to be best visible to them.

In general, this visual behaviour has been referred as 'pseudofoveation' although Whittaker and Cummings used the term 'adaptive fixation' (Whittaker and Cummings 1990). More recently, Crossland et al. (Crossland et al. 2004c) showed that AMD patients could learn to re-reference their oculomotor system over time without any active intervention and this was proven to have a beneficial effect on reading ability of these patients.

Awareness of the PRL location

One proposed method to use eccentric viewing was the afterimage method. The optimal viewing angle of the target was determined clinically first and then a strobe light was flashed at this retinal area. Then, the patient was instructed to superimpose this after image on a variety of targets. Alternatively, the patient can be asked to track moving objects. A case series using the latter method showed a subjective improvement in the patients receiving training (Holcomb and Goodrich 1976).

Similarly, an SLO can be used in order to identify the PRL used by the patient to fixate the target and the examiner can subsequently, increase the awareness of that area (Schuchard et al. 1994).

Using an optimal PRL

One of the goals of vision rehabilitation is to help AMD patients to establish an appropriate PRL and to use it efficiently (Rubin 2001). However, it is not clear if training is more effective than simple advice and practice.

Several methods have been used to teach patients to use their optimal PRLs. Nillson et al referred to them as 'TRLs' or trained retinal loci (Nilsson et al. 1998). Goodrich et al has used reading cards with horizontal bars in between each line of text to facilitate maintenance of the eccentric viewing angle (Goodrich et al. 1985), while other groups proposed computer based systems (Nilsson et al. 1998). A modified typoscope was also used in order the patient to keep macular fixation at a target while reading text at an eccentric location (Collins 1987). When combining with a steady eye strategy, the patient moves the page being read while keeping his fixation stable (Dickinson 1998).

Culham et al. (Culham et al. 1997) trained AMD patients to use an optimal PRL. As a result of a six- hour training patients demonstrated an improvement in distance and near acuity and fixation stability. However, there was no improvement in reading speed.

Nillson et al trained AMD patients aiming to shift their initial PRL vertically from the fovea to an area below their scotomas as that was judged as the best optimal area. Due to the fact that patients were also prescribed hyperocular reading spectacles at the initiation of the training, although an increase in reading speed was recorded, it cannot confidently be attributed only to training (Nilsson et al. 1998; Nilsson et al. 2003).

The use of prismatic spectacles

Prism relocation therapy is another way of redirecting the image away from the fovea onto the PRL. Patients are instructed to direct their fovea onto the object of interest in order for it to be presented at the PRL by means of prism. Initial research into this therapy showed impressive results where in one particular study an improvement in reading acuity was observed in 100% of subjects (Romayananda et al. 1982). However, similar improvement was recorded when a control group was also tested (94% versus 64%) by Rosenberg et al (Rosenberg et al. 1989). More recent studies found no real benefit for AMD patients in this therapy (Cacho et al. 2003; Smith et al. 2003).

Eye movement control

Eye movement patterns during reading are usually disorganised in AMD patients compared to normally sighted people (see chapter 3). Therefore, as an alternative to eccentric viewing strategy a different text presentation technique has been developed in order to facilitate the reading task for AMD patients. It is called rapid serial visual presentation (RSVP) and its aim is to present words one at a time in a fixed location instead of full page text. In this manner, no eye movements are necessary and it was hoped that the reading difficulties could be by-passed. However, studies showed that there was only a 40% improvement by using this technique (Rubin and Turano 1994), which was indicative of the fact that additional factors account for reading impairment in AMD (chapter 3).

Training of saccadic eye movements in patients with AMD was also attempted. But only a limited improvement was observed in reading rate in some of them after a seven-week rehabilitation program. Furthermore, no control group was used in that study (McMahon et al. 1993).

CHAPTER 2

BINOCULAR VISION

2.1. General aspects of binocular vision in normal subjects

Certain aspects of binocular vision need to be defined initially in order to understand its underlying physiological and psychophysical mechanisms in normal adults.

The line that joins the object of interest and its image on the retina is called *line of visual direction*. When this line connects the object with the fovea it is called *principal visual direction*, while connecting with all the other retinal elements give rise to *secondary visual directions*. When the subject fixates binocularly there are two lines of principal visual direction arising from the two foveae connecting them to the object of interest. Moreover, the object of interest is projected in the median plane of the head and not in any of the principal directions. This common direction is called *common subjective visual direction* of the foveae and belongs to both eyes. Furthermore, every retinal point in one eye shares a common visual direction in the other eye (von Noorden and Campos 2002). So although we use two eyes to 'see', the world is perceived as single and not double. Therefore, binocular vision can be represented by a single eye instead of two; *the cyclopean eye*. The cyclopean eye is an imaginary eye situated midway between the two eyes.

Retinal correspondence and retinal disparity

Retinal elements of the two eyes that have the same horizontal and vertical distances from the two foveolas are called "corresponding retinal points". By definition these elements have a common visual direction and when an object is placed there it stimulates corresponding areas and the two images of the object can be fused and perceived as one. The existence of retinal corresponding points forms the law of sensory correspondence in addition to the law of motor correspondence, which will be discussed later. Both of them describe the basic rules of binocular vision.

All the other retinal areas are "non corresponding" and have different visual directions. These retinal points are called disparate points and stimulation of these points lead to "retinal disparity", which is the basis of depth discrimination. Retinal image disparity occurs due to the lateral displacement of the eyes.

The Horopter

The horopter is the locus of points in visual space that stimulates corresponding points and lead to single vision. It was in 1613 when Aguilonius first (von Noorden and Campos 2002) used the term of 'horopter' to define the existence of a set of binocularly corresponding points lying on a circle in the horizontal plane of the head that passed through the optical centres (nodal points) of the two eyes and the single point of fixation. When the point of fixation was near the observer the circle was small and when the point of fixation was further away the circle was large. He mainly described a 'geometric' horopter, which was used later on by Vieth in 1818 and by Muller in 1840 and it is now called Vieth-Muller geometric horopter. The Vieth-Muller circle is a theoretical horopter. All points on this circle stimulate corresponding points on the retina and lead to single vision, provided that the fixation point lies on the centre of the circle and the eyes rotate about its nodal point (instead of their centre of rotation). The Vieth-Muller circle assumes there is angular symmetry of the corresponding points (Figure 2.1).

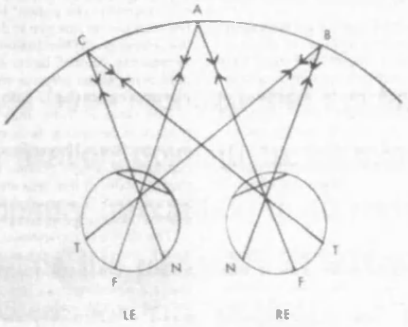


Figure 2.1. Vieth-Muller circle. Objects A, B, C and subsequently all objects on the circle stimulate corresponding retinal points on the two retinae (T, P, N) (Adler 1987).

Because the two eyes are separated horizontally each eye has a slightly different view of the world. Images lying in front or behind the horopter cause horizontal image disparity. In that respect all the corresponding points on the horopter have zero binocular disparities. By using several techniques to plot the

horopter perceptually (longitudinal horopter) it was noted that it was flatter than the geometric one which indicated that the distribution of corresponding elements was not symmetrical in the nasal and temporal retina of the two eyes. The deviation between the two horopters is known as Hering-Hillebrand deviation and it has been attributed to many factors, both neural and optical. As the nasal hemi-retina contains more photoreceptors at any given eccentricity per unit area compared to the temporal hemi-retina this produces a deviation in the horopter mapping in the visual cortex (Adler 1987). Furthermore, prismatic distortions of off axis rays, which pass though the lens of the eye, also flatten the horopter (Adler 1987). Moreover, there are changes in the shape of the horopter at different viewing distances. The horopter flattens as the fixation points recedes.

Panum's area of single binocular vision

When an object moves in front or behind the horopter it will stimulate non corresponding (disparate) regions on the two retinas. If this disparity is small the image of the object is still perceived as single. The region in of front and behind the horopter in which single vision is present is known as *Panum's fusional area* (von Noorden and Campos 2002). Thus, for any point on one retina there is a small area of points on the other eye, stimulation of which will lead to fusion of the two monocular inputs. Within this area single vision is possible and visual objects can be perceived stereoscopically (in depth).

It has been reported that the horizontal extent of Panum's area is narrowest at the fixation point (6 to 10 minutes at the fovea) and increases towards the periphery (around 30 to 40 minutes at 12° from the fovea). It becomes broader towards the periphery at a rate of 1 to 2 min of arc per degree of visual field eccentricity. The increase of Panum's area towards the periphery may be related to anatomical and physiological differences known to exist between the monosynaptic foveal cone system and the rod and cone system of the periphery. It parallels the increase in size of retinal receptive fields towards the retinal periphery and hence, it matches the increasing coarseness of peripheral vision. Moreover, it prevents peripheral diplopia when fixating a flat target held at close range. More recently, larger disparities of 2° to 3° have been shown to be fused by using randon-dot stereograms (Hyson et al. 1983; Erkelens and

Collewijn 1985; Piantanida 1986). Additionally, cyclofusion is possible despite cyclovergence errors of as much as 2 degrees between the two eyes.

Panum's area is not fixed in size (its size depends on spatial and temporal frequency of stimulus-size, sharpness and speed of the stimulus). Large, blurred, slowly changing images remained fused over a much greater range (Panum's area can be even 20 times wider) than small, sharply focused, rapidly changing images. It has been calculated that the largest disparity that can be still fused varies for steady eyes from 1.5 to 20 arc min according to spatiotemporal properties of target. When the eyes move during natural head motion the Panum's area width can expand to 150 arc min (2.5 degrees) (Adler 1987).

Fusion: sensory and motor fusion

Sensory fusion is defined as the unification of visual excitations from corresponding retinal images into a single visual perception. Both central and peripheral retina contributes to fusion. For sensory fusion to occur, apart from the images falling on corresponding retinal elements, they should be sufficiently similar in size, brightness and sharpness. Unequal images are a severe obstacle to fusion (von Noorden and Campos 2002).

Motor fusion refers to the ability to align the eyes in such a manner that sensory fusion can be maintained. The stimulus for these fusional eye movements is the retinal disparity outside Panum's area and the two eyes move in opposite directions (vergences). Unlike sensory fusion, motor fusion is an exclusive function of the extrafoveal retinal periphery. No stimulus for motor fusion exists when the images of a fixed visual object fall on the fovea of each eye (von Noorden and Campos 2002).

Requirements for binocular single vision (BSV)

In brief the requirements for binocular single vision (BSV) are the following:

a) Normal visual function in both eyes in order for the two perceived images to be sufficiently similar in size, brightness and sharpness. Unequal images can inhibit BSV.

b) Precise coordination of two eyes for all direction of gazes so images of the object will be received on corresponding areas of the two retinas.
c) Ability of the brain to promote fusion of two slightly dissimilar images.
This synthesis also results in three-dimensional vision which gives rise to depth perception (stereopsis). But stereopsis is not a requirement for normal binocular single vision.

Advantages of binocular vision

a) *Larger field of vision*

Viewing with both eyes provides a larger field of vision. When the two eyes are used together their visual fields overlap about 120° and this is called binocular visual field. Lateral to this field from both sides are crescent shaped monocular visual fields seen by each eye alone and they are measured at about 30° each. In summary the width of the total visual field when both eyes are used is 180° in contrast to the monocular visual field which is 150° in the horizontal plane.

b) *Stereopsis*

As the two eyes are separate horizontally at an interocular distance of 60-65mm, their retinal images of the object of attention are slightly different. It is this difference between the two images perceived from the two eyes that produces the perception of stereoscopic depth. Using stereopsis we can determine the relative position of the objects around us.

c) *Binocular summation*

If a visual task can be performed better with two eyes than with one this is a sign of binocular summation of the inputs to the two eyes. In that respect, visual thresholds seem to be lower when both eyes are used instead of one. Although it is accepted that binocular performance is better than monocular, the magnitude of this advantage varies and in many cases the advantage of having two eyes is relatively small (see next section on binocular summation for more details).

Binocular vision and stereoacuity with age

Many investigators have evaluated the general changes in binocular vision parameters and how they are related to symptoms in different age groups. Age related changes have been associated with a moderate increase in nearpoint heterophoria. Eames and Cambridge (Eames and Cambridge 1933) as early as

in 1933 reported that older patients (40 years old and over) were more exophoric than the younger group especially for near (mean: 7 prism diopters for near vision versus 0.39 prism diopters for distance vision) and other researchers verified their results (Sheedy and Saladin 1975). It was indicated that the amount of near exophoria was increased by about 1.5 prism diopters for every 20 years of age (Snydacker 1962). However, as the disparity vergence system remained constant throughout life, this increased exophoria seemed to be well compensated by the vergence system. Thus, presbyopic patients seldom complain of symptoms at a near working distance when reading through their reading aids.

A marked decrease in stereopsis has been reported for subjects beyond 60 years of age (Brown et al. 1993). More recently, Rubin et al (Rubin et al. 2001) demonstrated that visual acuity, contrast sensitivity and visual fields decreased at an approximately constant rate with age, whereas stereoacuity remained constant into the mid-70s but showing an accelerating decline thereafter. Specifically, they reported that stereoacuity threshold was 1.94 ±0.53 log seconds of arc in age group 65-69 year-old, increasing to 2.18±0.58 log seconds of arc in age group 80-85 year-old. Overall, the prevalence of stereoblindness increased from 10% in the 65 to 69 age group to 26.3% in the 80 to 85 age group. When there was a difference of three or more lines in visual acuity and contrast sensitivity, there was a sharp rise in stereoacuity thresholds, while when the difference was five to more lines almost all participants were stereoblind. Similarly, Haegerstrom-Portnoy et al. reported a decline in stereopsis with old age (Haegerstrom-Portnoy et al. 1999). The SKI study (Brabyn et al. 2001) described that older individuals' mean values were worse than young normal individuals across age by 34sec arc regarding stereopsis, with the decrease in stereopsis by a factor of almost 2 up to the age of 78 and by a factor of 7 at the age of 87.

The underlying mechanism by which stereopsis declines with age is not well known. Rubin et al. (Rubin et al. 1997) reported that amblyopia was not an explanation as from previous studies the prevalence of amblyopia was 7% for children and 3% for older adults. They hypothesized that the different vision loss (in visual acuity and contrast sensitivity) between the two eyes played a

more important role in decreased stereoacuity than an equal visual loss in both eyes (Legge and Gu 1989).

From other studies it has been shown that binocular summation for contrast detection in the fovea was lower in older normal subjects. Further analysis suggested the possibility that this was due to a larger relative loss in binocular sensitivity in old age. Likely selective loss of binocular neurons mediating peripheral sensitivity in the ageing eye was implied by Pardan et al (Pardhan and Whitaker 2003).

2.2. Binocular summation and inhibition

When the inputs of the two eyes are combined the resultant binocular interaction can be characterized by the comparison of the binocular performance on a task to the performance of either eye alone. *Binocular facilitation* is demonstrated when binocular performance (BP) is greater than the sum of the two monocular performances (MP); *complete summation* when BP is equal to the sum of the two MPs; *partial summation* when BP is better than MP but not twice as good and *binocular inhibition* when BP is worse than either eye alone (Steinman et al. 2000).

Steinman et al (Steinman et al. 2000) reported that summation or inhibition depended on the alignment or misalignment of the stimulus on the receptive field, concluding that summation occurs whenever corresponding parts of the receptive field are stimulated.

Theories of binocular summation of the visual system

There are two main theories that attempt to explain the advantage of using two eyes instead of one to perform a task; the probability and neural summation theories (Arditi 1986).

Probability summation theories

Superior binocular performance can occur on the basis of probability summation alone. The basic concept is that an improvement in binocular versus monocular performance can be expected because the simultaneous presentation of inputs to both eyes gives two opportunities for detection of the

stimulus. In that respect, this model asserts that the binocular condition is the same as if one eye received two successive stimulations. This theory is called *probability summation* theory and predicts that the two eyes have an independent opportunity to detect the presence or absence of a threshold stimulus and therefore, the binocular probability to detect the stimulus is described by the formula:

Pb = (1-probability that neither eye detected the signal), and thus

Pb = 1-(1-Pl) (1-Pr),

where Pb is the binocular probability of detecting the stimulus, Pl is the probability of detecting the stimulus with the left eye and Pr is the probability of detecting the stimulus with the right eye (Pirenne 1943). According to this formula if Pr=Pl=0.5 (for a 2-alternative task) the Pb is 0.75, which represents a binocular advantage over monocular of 25%. This theory suggests that binocular advantage could simply be a matter of statistics as with two sensors, you have a greater probability of detection than if you had just one.

Eriksen in 1966 (Blake and Fox 1973) suggested that the above model tends to overpredict the level of binocular performance expected from two independent chances to perceive the stimulus as a guessing component can be involved when the subjects fail to detect the stimulus by either eye. By applying the standard correction for guessing the resulting model is the two-state high-threshold or decision-threshold model which simply assumes the subject to be in either a correct-perception state or a guessing state. According to this theory, Eriksen and Green (Arditi 1986) proposed a binocular advantage of only 19% over monocular viewing. However, more work in that area suggested that sensitivity varies continuously and is represented by many states and not only two. A multistate model is designed in order to take into consideration several different subjective states of confidence about judgements of stimulus presentation (Blake and Fox 1973). Later a new model was proposed within the framework of signal detectability theory, which is known as the integration model. This model predicts the overall binocular sensitivity resulting from independent measures of sensitivity by combining the two monocular sensitivities according to the formula: $d_{bin} = \sqrt{\sum d_{mon}^2}$ (Blake and Fox 1973).

In all probability summation theories it is suggested that some detection decisions are made before the two inputs are combined. In contrast, the neural summation theory implies that monocular inputs combine first and afterwards the decision process begins (Arditi 1986).The core distinction between the two theories is mainly the level where the combination of the two monocular inputs takes place and the stage where the observer's response is established.

Neural summation theory

According to neural summation theory each monocular pathway carries equal energy to a common central pathway, where there is a convergence of the two monocular inputs. Each monocular pathway delives x amount of energy to a common central locus; the binocular system has 2x energy for carrying out the binocular task (Blake and Fox 1973). Therefore, binocular performance should be the same as if the stimulus has been presented to one eye twice and a binocular advantage of 100% over monocular should be demonstrated if this energy is utilised efficiently (Arditi 1986; Gilchrist and Pardhan 1987).

Campbell and Green (Campbell and Green 1965) suggested that binocular summation should decrease visual threshold by a factor of 1.4. They said that by combining the input from two eyes, neural signals would be added while background neural noise (assumed to be random and uncorrelated) should partially cancel. They predicted that this process alone would cause binocular thresholds to improve by a factor of $\sqrt{2}$ or 1.4. Although initially, it was treated as a probability model, they suggested that their model requires the actual physical summation of signals from the two eyes, which implies a neural summation model (Blake et al. 1981). Therefore, a 1.4-fold improvement in visual function could be explained by either probability or neural summation, but an improvement by more than this would strongly indicate that neural summation or some other form of physiological summation is involved.

In real life, binocular performance produces binocular summation in excess of probability summation which implies neural interaction. It is possible that binocular summation might be due to both probability summation and some physiological mechanism that further enhances binocular vision such as the neural summation implies and therefore, both models could be used to explain

the binocular advantage. Most of the research work presented in this field shows an overall binocular summation of 33-55% (Gilchrist and Pardhan 1987).

Studies on animal models based on cortical cells stimulation reported various outcomes of binocular performances including summation, facilitation or inhibition (Crawford and Cool 1970; Li and Creutzfeldt 1984; Ohzawa and Freeman 1986). It has been shown that not only more cells were stimulated during binocular interaction but also that they became more sensitive to binocular stimuli (Anzai et al. 1995).

In general, binocular summation was defined as an increase in binocular performance compared to that of each eye alone (Blake and Fox 1973; Blake et al. 1981). Binocular summation has been demonstrated in detection, recognition or magnitude judgments. When corresponding points in the two retinae are stimulated simultaneously, binocular summation normally results in improved visual acuity and contrast sensitivity. Binocular summation has been measured for acuity and contrast detection tasks as shown below.

Binocular summation and visual acuity

Various factors seem to influence the magnitude of binocular summation. As a general rule maximum binocular summation occurs when monocular sensitivities are equal and the binocular advantage has been calculated to range from 10% to 12% under high luminance and high contrast conditions (Campbell and Green 1965; Home 1978; Cagenello et al. 1993; Rubin et al. 2000). More specifically, binocular visual acuity in normal subjects was better than best monocular acuity by 11%, when contrast was the same in the two eyes. When contrasts were unequal in the two eyes, binocular acuity varied in accordance with the eye which received the higher contrast. In most but not all cases binocular visual acuity was still better than the monocular acuity of the eye that received the higher contrast (Cagenello et al. 1993) but the magnitude of the improvement decreased as the contrast disparity became larger.

Binocular summation and contrast sensitivity

Binocular performance for contrast sensitivity measurements was shown to be increased by 42% compared to monocular performance across all spatial

frequencies (Blake and Fox 1973; Blake et al. 1981). Unequal monocular contrast sensitivities such as in cataract or in amblyopia reduced binocular summation (Pardhan and Gilchrist 1991; Pardhan and Gilchrist 1992). A theoretical model to describe binocular contrast summation has been proposed by Legge (Legge 1984). According to this model, binocular contrast sensitivity is calculated by the following formula: $C^2 = Cl^2 + Cr^2$ (Cl=contrast of stimulus presented to the left eye and Cr= contrast of stimulus presented to the right eye). This type of summation is referred to as quadratic summation and it applies only to stimuli that when presented to the two eyes only differ in contrast.

Other important parameters that can affect binocular summation are the age of the subject and the spatial frequency tested (Pardhan 1996), the presence or absence of fixation disparity (Jenkins 1994), the presence of retinal correspondence, and the orientation and signal energies of the two monocular stimuli (Thorn and Boynton 1974; Blake and Levinson 1977).

Binocular summation in the peripheral retina

Although most of the studies on binocular summation have investigated the foveal region, there is a handful of reports exploring summation in the peripheral retina in normal subjects and in patients with ocular pathology.

Wood et al. (Wood et al. 1992) investigated binocular summation in relation to retinal eccentricity and target size in young normal subjects during a contrast detection task for spot targets of three different sizes (Goldmann equivalent I, III and IV) projected onto a perimeter bowl. He reported that by using a 0.108° target (target size I) binocular summation decreased with eccentricity. With a 0.431° target (target size III), summation remained constant and with a larger target (1.724°- target size IV) an increase in binocular summation was observed with increasing eccentricity. Binocular summation ratios at the fovea were not statistically different for either target size.

A study by Pardhan (Pardhan 1997) compared binocular summation at various eccentricities in young and older normal subjects and reported similar ratios in the fovea and the periphery, with older subjects showing lower ratios at all

eccentricities. Previously, in another study (Pardhan 1996), binocular summation ratios for contrast sensitivity in the fovea were higher at two spatial frequencies (1 and 6 c/deg) for the young normal group compared to the older group. Moreover, binocular summation ratios in young subjects were not statistically different in either spatial frequencies compared to the older group who demonstrated a spatial frequency dependence (1.31 and 1.13 at 1 c/deg and 6 c/deg respectively).

More recently, Pardhan and Whitaker (Pardhan and Whitaker 2003) reported no statistically significant difference in binocular summation ratios in young subjects at the fovea and periphery for contrast detection at spatial frequencies 1 c/deg and 4 c/deg. However, lowest binocular summation ratio was shown with older subjects for gratings of 4 c/deg in the periphery. Their results suggested the possibility of a larger relative loss in binocular sensitivity due to selective loss of binocular neurons mediating peripheral sensitivity in the ageing eye.

Pardhan (Pardhan 2003) also measured spatial frequency thresholds for recognition for binocular and monocular viewing conditions at two contrast levels (95% and 7%). Measurements were obtained at the fovea and at four different eccentric retinal locations (8° from the fovea on the horizontal axis and the other three in the superior field on retinal axes of 90°, 45° and 135°). For the superior and horizontal retinal locations, the orientations of the gratings tested were horizontal (180°) and vertical (90°). For the retinal points on the oblique axes, the orientations of the gratings were 45° and 135°. At the fovea, binocular summation ratios showed no significant differences for gratings of either contrast level or for any orientation. In the superior periphery, significantly higher summation ratios were shown for low contrast vertical gratings, and in the horizontal periphery for low contrast horizontal gratings. On the oblique axis, low contrast gratings that were parallel to the oblique meridian showed higher summation ratios compared to those at right angles to it. High contrast gratings did not show this effect. These data suggested that meridional organisation of the retina (e.g. vertical gratings seen maximally in the superior field) occurred for resolution and that it was evidenced closer to the fovea than previously shown.

Peripheral monocular grating resolution has been showed to be limited by the sampling density of the underlying retinal ganglion cells. According to Zlatkova et al. (Zlatkova et al. 2001) detection and resolution acuity for sinusoidal gratings were very similar in foveal vision and displayed a binocular improvement of 5% over best monocular acuity. However, in peripheral vision, while detection acuity improved by 6% binocularly, resolution acuity improved by 16%. This improvement was greater than predicted by probability summation and implies that the two monocular ganglion cell sampling arrays combine at a higher level resulting in a higher binocular sampling density. Although left and right eye visual fields overlap for 120°, binocular processing has also been shown to be reduced outside the central 40°. Grisby and Tsou (Grigsby and Tsou 1994) investigated binocular summation for gratings and flicker in the peripheral retina. Their results showed a large asymmetry between nasal and temporal retinal grating sensitivity in the far periphery especially at high spatial frequencies. A smaller asymmetry was found for flicker.

Binocular summation for grating acuity in the periphery was also studied in infants using a modified preferential looking procedure. Both binocular and monocular acuity increased between 2 and 11 months of age, but did not reach adult levels at the end of the first year of life. It was concluded that binocular acuity was always higher than monocular acuity and that acuity was higher in the temporal than in the nasal visual field at all ages (Sireteanu et al. 1994).

Binocular inhibition

Binocular inhibition occurs when the binocular performance is worse than monocular. In that respect, the worse seeing eye inhibits the performance of the better seeing eye and causes an overall reduction in the binocular visual function (Pardhan and Gilchrist 1990; Pardhan 1993).

Fechner's brightness paradox

Fechner in 1860 reported a paradoxical phenomenon which can occur when the two eyes are unequally illuminated by using a neutral density filter to see through the one eye. He observed that the binocular brightness of the viewing spot was less than its brightness when viewed monocularly by the unfiltered

eye. It appeared that binocular brightness was more like an averaging of two monocular inputs than a summation of those same inputs. This phenomenon is called "Fechner's Paradox". The same phenomenon also has analogues in other senses where pooling of two sensory inputs exists, such as in audition (Lehky 1983).

Gilchrist and McIver (Gilchrist and McIver 1985) showed an analogue of this phenomenon exists in contrast sensitivity. It is generally accepted that binocular spatial contrast sensitivity in normal observers is higher than monocular sensitivity by some 42% across all spatial frequencies, an amount predictable on the basis of neural summation of the two monocular responses. Such summation predicts that a reduction of sensitivity in one eye would result in a fall in binocular sensitivity to a level approaching, but never lower than, that of the other eye. They reported that reduction in monocular sensitivity caused by reduced luminance in some subjects produced lower binocular sensitivity to a level below that of the other eye. In other subjects the expected summation occurred and binocular sensitivity remained at or above the monocular level. As Blake and Fox (Blake and Fox 1973) had suggested, brightness summation possibly occurred when both eyes were 'identically' stimulated.

By using neutral density filters to produce unequal monocular sensitivities in a contrast detection task, Gilchrist and Pardhan (Gilchrist and Pardhan 1987) also found that binocular detectability was reduced to below that of the better eye. The magnitude of this phenomenon remained constant across the range of stimulus contrasts. Legge and Rubin (Legge and Rubin 1981) also reported similar binocular visual behaviour, when they presented images with different suprathreshold contrasts to the two eyes.

2.3. Binocular summation and inhibition in AMD

There is evidence of lack of binocular summation in many AMD patients (Fosse et al. 2001). There are two main factors to explain this behaviour (Valberg and Fosse 2002). Firstly, as was mentioned before, AMD can occur at different times in the two eyes and often presents with incongruous macular scotomas. In these cases, even if binocular retinal correspondence is preserved, unequal retinal stimulation could impair binocular summation. Recent studies (Curcio et

al. 2000; Owsley et al. 2000) indicated that rods are more vulnerable to early damage than cones. This can possibly lead to the same effect as unequal light adaptation of the two eyes according to Valberg and Fosse (Valberg and Fosse 2002). As AMD affects central vision under these circumstances visual acuity, contrast sensitivity and stereopsis could be affected (Valberg and Fosse 2002). Further more, additional eye disease such as unilateral cataract or monocular pseudophakia can co-exist with AMD and thus produce dissimilar retinal illumination of the two eyes.

Faubert and Overbury (Faubert and Overbury 2000) reported that AMD patients often demonstrated worse binocular sensitivity to spatial information, as measured by spatial contrast sensitivity, than when the stimuli are viewed with only one eye. This "inhibition" was not related to the contrast sensitivity of the better eye or to the visual acuities but it was more obvious primarily in images with medium to low spatial frequency components (medium to large size bars). For visual acuity measurements in AMD Rubin et al showed (Rubin et al. 2000) that there was little evidence for binocular inhibition when the monocular acuities in the two eyes were unequal and measures of monocular acuity could accurately predict binocular acuity.

2.4. Binocular rivalry and suppression

When different images are presented to the two eyes at corresponding retinal points, their excitations are localized in the same visual direction and they compete for perceptual dominance. As fusion is impossible, one image or the other is temporarily 'suppressed'. This phenomenon is called retinal rivalry. As a consequence of this rivalry one eye's view dominates for several seconds and then is replaced by the view of the other eye. Because of this competition and the inhibition elicited, only fragments of the image are seen by each eye. If the dissimilar images are small in area, then the entire image of the target in each eye can alternately suppressed and this phenomenon is called *exclusive dominance*. If larger dissimilar stimuli are presented, a mosaic of the two images is perceived and its contour continuously changes over time as there is a constant local competition and alternation at each location of the image. The latter is called *mosaic dominance* (Steinman et al. 2000) and these independent areas of alternation are called spatial zones of binocular rivalry (Blake et al.

1992). They have similar size to the portion of visual field processed by a cortical hypercolumn and therefore, the spatial size of the zone of binocular rivalry will increase further as more peripheral areas of the visual field are excited by dissimilar stimuli. Moreover, it has been reported that when one views an array of spatially distributed rival targets, a combination of left eye and right eye targets appears to be dominant simultaneously (Kovacs et al. 1996). It has also been reported that it takes up to 150msec (Schor et al. 1976) before dissimilar visual input to the eyes causes rivalry although it has been shown that this time to be shorter for dichoptic stimuli (Leonards and Sireteanu 1993).

The basic mechanism of binocular rivalry is not clearly understood. It is claimed that there are separate neural channels for the right and the left eyes that compete for access to the visual cortex while a third binocular channel is activated only by fusible input (Cogan 1987). Competitive interaction occurs not only at the primary visual cortex (Blake 1989) but also through interactions between binocular neurons at several afferent levels of the visual pathway well after the inputs of the two eyes have converged (Leopold and Logothetis 1996; von Noorden and Campos 2002).

What conflicts during binocular rivalry has been investigated by many research groups, as it is important to know what dominates in this situation; a specific stimulus or the retinal region where the dominant stimulus is imaged. It has been shown that a visually stronger stimulus is less likely to be suppressed during rivalry and is visible a greater proportion of the time than when a weaker stimulus is used, as reported by Levelt in 1965 (Steinman et al. 2000). It also appears that the degree of inhibition remains stable through the 'suppression' period (Fox and Check 1972). The phenomenon of retinal rivalry can also be caused by uniform surfaces of different color or unequal illumination of the two targets and there are many reports in the literature of different combinations of stimuli (von Noorden and Campos 2002). Chromatic stimuli seem to be suppressed to a greater extent than achromatic ones (Smith et al. 1982; Ooi and Loop 1994).

By contrast, a general review of the literature proves that it has also been demonstrated that eye rivalry dominates and which of the two images is

suppressed depends more on ocular dominance rather than the stimulus characteristics (Blake and Fox 1974; Blake et al. 1980; Blake et al. 1998). Logothetis et al (Logothetis et al. 1996) challenged the previous reports and from their work concluded that rivalry occurs between competing stimuli and not the eyes.

More recently, Lee et al. (Lee and Blake 1999) demonstrated that stimulus rivalry occurs only within a limited range of spatial and temporal parameters of the stimuli (low contrast, rapidly flickering targets), otherwise eye rivalry dominates. Moreover, as was described earlier, rivalry appears within local regions of the visual field and not involving the entire eye's view. Hence, when 'eye' rivalry is described it is referred to the dominance of these local regions by only one eye. Visual field asymmetries in the temporal characteristics of binocular rivalry have also been demonstrated, where rivalry was faster for stimuli presented at the lower than the upper visual field (Chen and He 2003).

In general, binocular rivalry is a constantly changing process, always requires competing stimuli in each eye. Stereopsis can be preserved during rivalry. Cessation of rivalry due to constant foveal suppression of one eye leads to complete sensory dominance of the other eye, which is a major obstacle to binocular vision. Return of binocular rivalry is a requisite for reestablishment of binocular vision.

Suppression during binocular rivalry

When conflicting images are presenting to the two eyes the visual system can actively 'ignore' either part or the entire image from one eye. This is called *suppression under binocular conditions* and although it is referred to one eye only, it arises from binocular viewing and interaction. It aims to eliminate confusion which occurs when dissimilar stimuli are presented to the two eyes. The 'suppressed area' has reduced sensitivity to visual stimuli, elevation of light detection thresholds and prolongation of reaction times (Steinman et al. 2000). An example of binocular suppression is provided in figure 2.2 below.

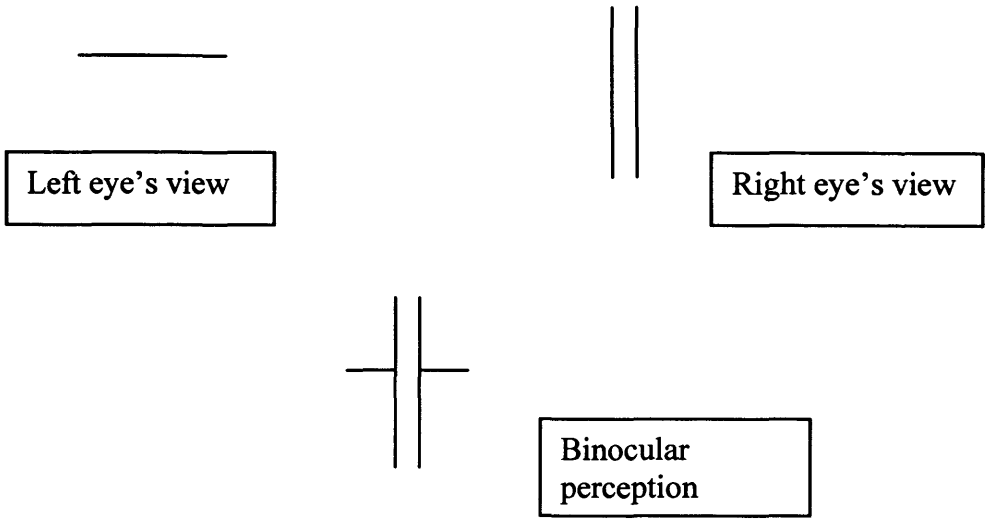


Figure 2.2. One straight line is presented to the left eye and two parallel vertical lines to the right eye. During binocular perception of these targets a part of the left eye's view is suppressed and the perception is an incomplete line intersecting the two vertical lines. When the right eye is covered again then the left eye sees one complete straight line (Foundations of binocular vision. A clinical perspective. (Steinman et al. 2000).

This figure showed an example of *local suppression* as the conflicting images in the two eyes were only localized and thus suppression occurred only in that area. This type of suppression is intermittent.

Suppression in strabismus

In strabismus the object of interest stimulates non corresponding retinal points and hence double vision is elicited. As a compensatory mechanism for diplopia children actively 'neglect' the disparate and confusing images originating from the retina of the deviating eye. The *suppression* is a temporary phenomenon as it occurs only when both eyes are open. When the fixating eye is covered, suppression ceases and the deviating eye takes up fixation. Suppression here can be alternating or strictly monocular. When there is continued monocular suppression of the squinting eye *strabismic amblyopia* can occur. Occasionally, young children with long standing strabismus can preserve some degree of binocularity by establishing *anomalous retinal correspondence* where the retinal elements of normal eye assume an anomalous relationship with the retinal elements of the deviating eye.

There is a lot of debate in the literature whether suppression is just an exaggeration of binocular rivalry. Smith et al. (1985) among others (de Belsunce and Sireteanu 1991) suggested that strabismic suppression and normal binocular rivalry suppression are mediated by different neural mechanisms while other research groups demonstrated that binocular rivalry is the basis for suppression (Harrad et al. 1996).

Do adults suppress?

It is general knowledge that strabismus acquired in childhood results in suppression of the diplopic image, whereas strabismus acquired in adulthood causes diplopia or conscious image ignoring, but not true cortical suppression. Von Noorden reported that the critical period during which suppression can develop ends at 8-9 years of age such as in amblyopia. If the ability for suppression is lost during adulthood it cannot be regained and double vision appears (head injury, surgical correction of strabismus etc). Despite this general view some research groups performed visual evoked potential responses (VEPs) during binocular rivalry in adults to further investigated this. Wright et al (1990) among other investigators (Lawwill and Biersdorf 1968; Kawasaki et al. 1970; Campos 1980) reported that adults with acquired strabismus have reduced electrical responses which meant that they do not simply "ignore" the diplopic image but they actually have a suppressed cortical visual activity. Data from children showed no recordings at all from the suppressed eye. In contrast, other authors failed to support this hypothesis (Cobb et al. 1967) using similar techniques.

Moreover, it has been well documented that as adults cannot suppress, they sometimes develop an abnormal head posture to compensate for double vision in the presence of strabismus. Alternatively, especially when the deviation is large and the 'second' image appears in the periphery of the visual field, the patient simply learns to 'ignore' this image instead of demonstrating suppression. This seems to occur at a psychological level and it depends on the attention value of the second image as it is dealt with in the perspective of physiological diplopia. In these cases, diplopia can be elicited by placing a light red filter in front of one eye (von Noorden and Campos 2002).

Global versus regional suppression

Very rarely suppression involves complete exclusion of the whole retina of one eye. Von Noorden reports that this can only be seen in exotropic patients with alternation (von Noorden and Campos 2002). In all the other cases suppression is *regional.* It usually occurs in the fovea and part of the periphery (where the stimulus is projected) of the deviated eye causing two functional scotomas or just in the periphery (in small angle strabismus). In alternating strabismus these scotomas can be found in one or the other eye depending on fixation. It takes less than 80msec to switch the fixation and suppression from one eye to the other (Steinbach 1981). The suppressed area in the visual field in one eye can also be complemented by the non-suppressed corresponding area from the visual field of the fixating eye.

CHAPTER 3

READING

Reading is an extremely complex task which requires good vision, stable fixation, accurate control of eye movements, adequate visual field, and the cognitive interpretation of the meaning of the text. Nevertheless, reading is important for full participation in society. As ageing occurs and mobility sometimes becomes defective a lot of older people depend on reading for their hobbies, communication and maintaining their independence.

Reading ability is disrupted in patients with AMD and difficulty in reading is reported to be the most common complaint in patients with AMD (Krieger 1967; Elliott et al. 1997; Hazel et al. 2000; Holz et al. 2003). Reading with central field loss requires most often requires utilization of peripheral retinal locus and thus it is fundamental to understand how the text is processed differently by the central (in normal subjects) and in peripheral retina (in AMD subjects). A brief summary of reading in normal sighted subjects and AMD patients will be presented below.

3.1. Reading in normal subjects

3.1.1 Reading speed

Experienced readers with normal vision generally read between 250 and 400 words per minute. The most important factor that determines reading speed is *letter size*. The maximum reading speed is achieved for letter sizes between 0.3° and 2° and this range seems to cover most of the ordinary print (Legge et al. 1985a). Reading speed is reduced rapidly for letters smaller than 0.3° as it approaches visual acuity limits. A more gradual decline has been recorded for letters larger than 2°.

Normal sighted subjects can tolerate considerable reductions in text *contrast* with little effect on reading performance. It has been shown that reading speed is reduced less than a factor of two when a tenfold reduction in contrast occurs (Legge et al. 1987). Reading speed is fairly constant for contrasts above 10% but for further contrast reduction there is more rapid decline in reading speed (Legge et al. 1987; Legge et al. 1990).

Contrast polarity (black letters on a white background versus white on black) has little effect on reading speed over a wide range of character sizes. There is about a 10% higher reading speed when black letters on white background are used (Legge et al. 1985a).

The *width of the visual span* can affect the reading speed of the reader. During reading several letters are processed during each fixation. The width of the 'window' of the characters seen in a single fixation is called visual span (O'Regan 1990; Legge et al. 1997). According to O'Regan its size depends on three factors; the size of the critical features in the letters, the fall-off in the eye's spatial resolution away from the fixation point and the geometry of the display surface. Based on these he designed a model that predicted that the maximum size of the visual span is 15.6 letters occurring for letter size near 1°(normal text) , while for letters subtending 6 ° (magnified text), the span was 10.4 letters. However, the visual span empirically measured by Legge et al. was different indicating that possibly different parameters should be taken into account. Specifically, he reported that the visual span was around 10 characters for 1° and 5.3 letters for 6° in subjects with normal vision reading high contrast text (Legge et al. 1997). Rayner et al by using a computer based eyetracking method to mask letters surrounding the point of fixation during reading also measured a visual span of 7-11 letters (Rayner and Bertera 1979), as when the mask covered the central seven letters reading speed was very low and when covering 11 letters reading was not possible. The limit for the window width visible is 4 letters independent of character size and below this limit reading slows (Legge et al. 1985a).

Many researchers have also investigated how much useful information can be acquired during each fixation and how big should be the region from which

useful information can be obtained during a fixation in reading. This is called perceptual span (McConkie and Rayner 1975; Rayner 1975). The span is asymmetric to the right for readers of English as it extends about 3-4 letters to the left of fixation and up to 15 characters to the right of fixation (Rayner and Bertera 1979; Rayner et al. 1980). Interestingly, the direction of asymmetry of the span is reversed in right-left languages (Israeli) with more letters read to the left of fixation and less letters to the right (Pollatsek et al. 1981), while in more complex languages such as Chinese the perceptual span is much smaller with 3 characters to the right of fixation (Pollatsek et al. 2000).

3.1.2 Eye movements during reading

During reading normal sighted subjects move their eyes across the text in a saccadic pattern interrupted by fixation pauses. Normal saccadic latencies for reading are around 250msec (Rayner 1978). Only the first 50ms is required to decode the visual stimulus (Morrison and Rayner 1981).The rest is mainly used to acquire semantic information from the text and combine it with previously read material as well as for programming subsequently eye movements. If the meaning of the words read is uncommon or ambiguous the fixation duration is increased (Raney and Rayner 1995).

Size and direction of saccades

For normal reading in English the mean saccade length seems constant with respect to the number of letters, usually about seven to nine characters which is well within the visual span. Long words may be fixated twice and shorter words can be skipped. The landing area for each saccade is usually located halfway between the beginning and the middle of the word (Rayner 1979a; McConkie et al. 1988).

As mentioned previously for reading at a normal rate we need to 'see' 3-4 characters to the left of fixation and 15 characters to the right of fixation at a glance (McConkie and Rayner 1975; Rayner and Bertera 1979). To the right of fixation, different types of information are acquired with information necessary for semantically identifying words limited to the foveal and near parafoveal region and more gross types of information acquired further into the parafovea (Rayner 1975).

If the text is presented one word over time to eliminate the need for saccadic eye movements reading speed can significantly increased. By using the RSVP technique (Rapid Serial Visual Presentation) (Forster 1970), Rubin and Turano (Rubin and Turano 1992) recorded reading speed of 1,652 words/min in normal subjects.

Regressions

About 10-15% of saccades are regressive saccades (right to left movements along the line or movements back to previously read lines). Regressions bring fixation to previously read text and they are thought to be due to difficulties in recognition or in comprehension of the text, especially if they are more than 10 letters spaces back.

Saccades to find beginning of next line

When moving from the end of one line to the beginning of the next line, normal readers often undershoot and make small corrective saccades to the left. Their first and last fixations on the line are normally 5-7 letter spaces from the end of a line.

3.2 Reading in AMD subjects

3.2.1 *Reading speed in AMD patients*

Patients with central visual loss due to dense scotoma at the macula demonstrate reduced reading speed (Legge et al. 1985a; Bullimore and Bailey 1995; Lovie-Kitchin et al. 2000). In these studies it has been reported that AMD subjects read slower than 70 words/min (median reading rates were 25 words/min). Bullimore and Bailey (Bullimore and Bailey 1995) proposed three critical factors to explain impaired reading speed in AMD patients. The first factor was the smaller perceptual span, the second one was the poor control of eye movements and the third component was associated with the subject's ability to integrate information within and across sequential fixations. Moreover, reduction in luminance can result in changes in scotoma size and shape with direct effect on visual acuity and reading speed (Bullimore and Bailey 1995).

Reduction in visual acuity alone cannot explain these low reading rates as these measurements were reported even when very large characters (12-24 degrees) were used to compensate for the reduced resolution (Legge et al. 1985a). Moreover, visual acuity was a poor predictor of reading speed in AMD patients as shown in many studies (Legge et al. 1992; Bullimore and Bailey 1995; Fletcher et al. 1999).

Moreover, contrast sensitivity impairment in AMD patients cannot solely account for reduced reading speed (Legge and Rubin 1986; Legge et al. 1992; Bullimore and Bailey 1995), although lower levels of contrast impairment are associated with better reading speed. Whittaker and Lovie-Kitchin (Whittaker and Lovie-Kitchin 1993) reported that a contrast reserve of 3:1 is required for fluent reading and a contrast of 11:1 for high fluent reading speed of 170 words/min.

Visual span in AMD

The presence of macular scotomas reduces the numbers of letters which can be seen in each fixation when the patient views directly on the text. By using simulated scotomas presented in the centre of the word Rayner and Bertera reported that reading speed was halved even when the mask was only one letter (Rayner and Bertera 1979).

Most often AMD readers use their PRL to scan across the text. The necessity to use peripheral retina impairs their reading performance. As has been already reported, visual resolution (Jacobs 1979) declines with retinal eccentricity. Fine et al (Fine and Rubin 1999a; Fine and Rubin 1999b) scaled the letter size to counteract for this and by using artificial scotomas they still found a significant reduction in reading speed even when a small mask size used. They reported that for scotomas sizes < 7.5 degrees the number of the letters masked had a more significant effect on the reading speed than the size of the mask *per se*.

However, by increasing print size the number of letters seen in each fixation is also decreased causing shrinkage of the visual span. Legge et al (Legge et al. 1997) reported that by increasing the print size by a factor of six the number of

characters in the visual span is halved. It has been reported that reading speed is negatively correlated with scotoma area (Cummings et al. 1985) but mainly for large scotomas. When patients were presented with smaller scotomas size this correlation was poor (Bullimore and Bailey 1995).

3.2.2 Eye movements during reading for AMD patients

Saccades, fixations, and regressions

By using eye movement recording techniques it has been demonstrated that AMD subjects show more fixations per word (Bullimore and Bailey 1995) than normal readers presumably related to a reduced visual span. Interestingly, they found no difference with respect to fixation duration compared to normals. On the contrary Legge et al (Legge et al. 1985a) showed an increase in fixation duration but in their study they included patients with a variety of pathologies causing low vision and not only AMD.

The time to initiate saccades is longer than normal (White and Bedell 1990). Whittaker et al also reported a mean saccadic latency of 402 msec in AMD patients while the normal controls had mean latency of 298msec (Whittaker et al. 1991). Bullimore and Bailey (Bullimore and Bailey 1995) reported shorter saccades between fixations than normal readers. Peak velocity of saccades is also reported reduced in AMD compared with normal age-matched subjects (Whittaker et al. 1991). In addition, AMD patients often undershoot the intended target (Whittaker and Cummings 1986). Regression saccades are also more frequent in AMD subjects than normals (McMahon et al. 1991; Bullimore and Bailey 1995).

In general, the performance of AMD patients in reading was reproduced by using simulated scotomas in normal subjects (Bowers and Reid 1997). Rayner and Bertera (Rayner and Bertera 1979) using the above technique described how a gaze-contingent mask which masked one letter of the word halved the reading speed.

Other additional factors that influence reading speed could be the ability of the PRL to maintain fixation stability and make efficient saccades. Previous studies have been reported that AMD patients accurately placed the reading text within

their PRLs but there were fewer letters per forward saccades and more regressions (Cummings et al. 1985; Bullimore and Bailey 1995). Schuchard et al (Schuchard and Fletcher 1994) also measured the "saccade to PRL" ability and this measurement was a better predictor of reading speed than visual acuity in patients with central visual loss.

Eye movement control is poor in peripheral retina in patients with central scotomas. If that was the main reason for impaired reading speed in AMD readers, the use of RSVP should be able to by- pass the problem and help AMD patients to reach almost normal reading speeds. Rubin et al (Rubin and Turano 1994; Rubin et al. 1997) using RSVP in a variety of low vision and normal subjects concluded that although peak reading speed improved (from a mean of 82 words/min to120 words/min) this improvement was smaller than for other low vision groups (from 182 to 389 words/ min) or for normal subjects (303 to 1171 words/min). Therefore, other factors seem to account for the reduced reading speed in AMD.

In conclusion reading speed is affected by many parameters in AMD patients. The reduction in visual span together with the poor control of eye movements in retinal periphery seem to be important factors to account for poor reading performance. Other important factors, that also play a role in reading, are the reduced visual acuity and contrast sensitivity in these patients.

PROJECT OVERVIEW

CHAPTER 4

4.1. Project Overview

In advanced age related macular degeneration (AMD) the patient develops a blind spot or scotoma in the most sensitive central area of the field of view, the fovea. In order to fixate a target, read or recognize faces most patients with AMD adopt an eccentric retinal locus that acts as a pseudo-fovea. This retinal area is called the preferred retinal locus (PRL). Many techniques have been employed to locate and evaluate PRLs throughout the previous years using different devices including scleral search coils (Cummings et al. 1985), fundus cameras (White and Bedell 1990; Nilsson et al. 1998) and mainly in recent years scanning laser ophthalmoscopes (SLOs), which will be described in more detail later. Although both of the latter devices depend on visualisation of the fundus, using the SLO a larger variety of fixation targets can be displayed including stationary (Timberlake et al. 1986; Schuchard and Raasch 1992; Guez et al. 1993), moving targets or even scrolled text (Culham et al. 1992). In addition by means of an SLO, the examiner is able to assess the relationship between the location of the PRL and the retinal scotomas which can be functionally mapped using the SLO microperimetry technique (see section 5.4.1).

However, all of the aforementioned studies have examined the PRLs under monocular viewing conditions and mainly using the patients' better eye. As far as we are aware there are only very limited reports of binocular viewing in AMD patients (Schuchard and Fletcher 1994; Schuchard et al. 1995; Schuchard et al. 2003). In summary, the above researchers suggested that some AMD patients demonstrated non-corresponding monocular PRLs, while in many cases binocular perception was impaired despite the presence of retinal correspondence.

AMD often affects the two eyes differently regarding the size and the location of the scotomas. This binocular incongruity may interfere with the development of the eccentric viewing, normal eye movement co-ordination and binocular

function. In that respect, eye movements cannot be studied accurately by studying each eye separately. The PRL in one eye does not necessarily correspond with the PRL in the other eye and it cannot be predicted which retinal locus will be used if the subject uses both eyes to view a target (figure 4.1).

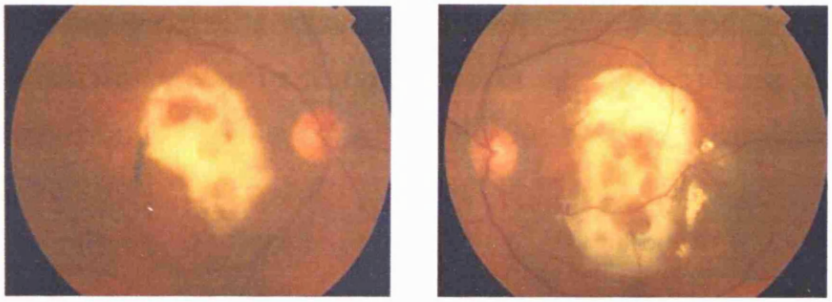


Figure 4.1. Colour photos of the posterior pole of a 60 year-old AMD patient with disciform scars on both maculae. Note the different size of the lesions.

The purpose of this study is to investigate the impact of symmetrical versus asymmetrical macular scotomas on the development and stability of eccentric viewing in patients with bilateral AMD and the potential of binocular function. The impact of these factors on the performance of visual tasks such as reading will also be evaluated. The results of this study will aid our understanding of patients' monocular versus binocular visual behaviour. They will also provide a useful insight into how people with bilateral scotomas operate in the real world. This information is essential for developing effective vision rehabilitation.

4.2 General hypotheses

Patients with bilateral AMD were recruited and divided into two groups based on the intraocular difference in their scotomas size: those with symmetric and those with asymmetric scotomas. It was hypothesized that:

Hypothesis 1: *AMD patients with symmetrical central scotomas are more likely to have preferred retinal loci with similar retinal eccentricities in both eyes under monocular viewing conditions than patients with asymmetrical scotomas.*

Our first hypothesis is based on the fact AMD patients tend to fixate very close to scotoma borders (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999) and thus patients with symmetrical scotomas are more likely to have monocular

PRLs in the two eyes that fall on more corresponding retinal areas than patients with asymmetrical scotomas.

Hypothesis 2: P*atients with asymmetrical scotomas are expected to use different PRLs under binocular versus monocular viewing in the worse eye. A shift in the PRL is expected in the worse eye under binocular versus monocular viewing conditions. However, in patients with symmetrical scotomas no shift in PRL is expected from monocular to binocular viewing. Therefore, patients are expected to use the same PRLs under both viewing conditions in both eyes.*

Hypothesis 3: *AMD patients will exhibit PRLs under binocular viewing conditions with similar retinal eccentricities between the two eyes. These PRLs are likely to fall on corresponding retinal areas in the two eyes. No difference is expected in patients with symmetrical versus asymmetrical scotomas with respect to retinal correspondence of binocular PRLs.*

Hypothesis 2 and 3 are based on the clinical observation that some AMD patients change their eye position and/ or head position when they are asked to perform standard clinical tests monocularly, e.g. testing distance acuity using a Snellen chart in the clinic, compared to their position when they are looking at a target with both eyes. Moreover, we had no clinical observation of AMD patients seen in the medical retina clinics that had developed manifest squints after the onset of their ocular condition.

Hypothesis 4: *Fusion is expected to be preserved in patients with corresponding PRLs that fall outside the scotomas. Therefore, fusion should be preserved in patients with symmetrical scotomas but not in cases with asymmetrical scotomas.*

As fusion is a bilateral phenomenon, ocular alignment and an adequate sensory input from both eyes are essential.

Hypothesis 5: *Clinical performance is expected to be superior under binocular viewing conditions compared with the performance using the better eye in patients with symmetric scotomas. Clinical performance is expected to be equal*

or worse under binocular viewing conditions compared with the performance using the better eye only in patients with asymmetric scotomas.

As we assumed that patients with symmetrical scotomas would use corresponding PRLs under both monocular and binocular viewing conditions, binocular summation is expected in their clinical performance as with normal sighted subjects. However, in patients with asymmetrical disease, their performance is expected to be different under the two viewing conditions.

Evidence of binocular inhibition has been previously reported for unequal monocular sensitivities such as in cataract or in amblyopia (Pardhan and Gilchrist 1991; Pardhan and Gilchrist 1992). The lack of binocular summation and the presence of inhibition in AMD patients regarding clinical tests, such as contrast sensitivity, have previously been reported (Fosse et al. 2001). Based on the same rationale we constructed hypothesis 6.

Hypothesis 6: *Reading speed in patients with symmetric scotomas is expected to be better under binocular versus monocular viewing conditions. In contrast, patients with asymmetric scotomas are expected to behave similarly under monocular and binocular viewing conditions.*

4.3 Project Protocol

1. *Distance Visual Acuity*

   Distance visual acuity was measured binocularly and monocularly using the ETDRS logMAR chart.

2. *Reading acuity*

   Reading acuity was recorded using the MNRead acuity cards. Binocular and monocular measurements from each eye were obtained.

3. *Contrast sensitivity*

   Contrast sensitivity was assessed using the Pelli-Robson letter chart. Measurements were obtained for each eye separately and for both eyes.

4. *Assessment of binocular function*

- Cover test
- Test for simultaneous binocular perception
    - Simultaneous binocular perception was tested using the Bagolini striated glasses by using a "full field" streak.
    - A test using a dichoptic fixation target by means of CrystalEyes system was used to test simultaneous binocular perception in more localised areas such as at the fixation locus and immediate area outside macular scotomas.

  If there was no binocular perception present in the above tests, there was no need to perform the following stereoacuity test. Instead, we directly proceeded to test no 5.
- Stereoacuity test

  The Frisby test was used to assess stereoacuity.

5. *Mapping of the physiological blind spot*

   Psychophysical maps of the blind spot were created monocularly using an infrared eyetracker and a scanning laser ophthalmoscope (SLO). The distances between the centre of the blind spot and fixation locus (PRL) were compared in order to prove that the subject uses the same retinal locus to fixate monocularly under both experimental conditions. The experiments were performed with normal controls and AMD subjects.

6. *Documentation of changes in gaze position under monocular versus binocular viewing.*

   A SMI Eyelink Gazetracker was used to record gaze position changes under monocular versus binocular viewing conditions, when the patient fixated a simple target presented on the computer monitor. Data were obtained from both eyes. Comparison between monocular and binocular recordings determined if the subject used the same PRL for both experimental conditions. Fixation stability and the number of possible PRLs for each eye were also identified when viewing monocularly and binocularly.

7. *Identification of monocular PRL and mapping of macular scotomas.*

   The preferred retinal locus (PRL) was identified monocularly for each eye

using a Scanning Laser Ophthalmoscope. Macular scotomas were mapped in both eyes using the SLO microperimetry technique in order to assess scotoma location, size and its relationship to the identified PRLs.

8. *Prediction on fixation locus used under binocular viewing on SLO images*
   Combination of binocular fixation data from the eyetracker and monocular SLO fixation data predicted the retinal locus used for fixation under binocular viewing conditions for both eyes. Moreover, the correspondence of binocular PRLs and their position with respect to the macular scotomas were assessed.

9. *Reading*
   Reading speed was investigated when reading with both eyes versus reading with the better eye. Using the infrared eyetracker eye movements were recorded while reading standardised text presented on a computer monitor under both viewing conditions. Number of saccades and regressions, saccade size, fixation duration were analysed during silent reading.

The statistical software used throughout this project was JMP version 5.1a.

GENERAL METHODS AND INSTRUMENTATION

CHAPTER 5

5.1 RECRUITMENT OF PATIENTS

Inclusion and exclusion criteria

All patients were recruited from the medical retina clinics at Moorfields Eye Hospital. Normal controls were colleagues, friends and relatives of recruited patients.

Inclusion criteria

Patients with bilateral AMD were included in this study. All patients had macular pathologies that were positively diagnosed by ophthalmoscopy and had to have stable pathology clinically and subjectively for longer than one year. Distance visual acuity with best refractive correction had to be better than 1.3 logMAR on the ETDRS chart in both eyes, as worse acuity was likely to limit the ability of the patients to perform some of the tests.

Exclusion criteria

Patients were excluded if there was a history of additional ocular disease that could affect visual acuity, except for minor cataract. Patients were asked specifically for a history of squint or amblyopia and if it was reported they were excluded from the study.

Inclusion criteria for control subjects

Controls subjects were age-matched and they had no history of eye disease in either eye (except for minor cataract). Distance visual acuity with best refraction had to be at least 0.1 logMAR in both eyes.

Ethical Committee approval

The study was approved by the local ethics committee (Moorfields Eye Hospital) and the tenets of the Declaration of Helsinki were followed. Written informed consent was obtained from all subjects before the commencement of the examination session. The consent form used is attached in appendix 1.

5.2 TESTS FOR ASSESSING VISUAL FUNCTION

5.2.1 Distance visual acuity test

Distance acuity was measured using the ETDRS charts (charts developed for the Early Treatment Diabetic Retinopathy Study) (Ferris et al. 1982) .The charts conform to standards for acuity testing proposed by the National Academy of Science-National Research Centre Committee on Vision (1980). The chart was transilluminated with the Lighthouse Chart illuminator (The Lighthouse International, New York) to a level of approximately 130 candela/m^2 (cd/ m^2). Visual acuity was tested at a distance of 4m with habitual refractive correction for distance. If the patient was unable to read the largest letters on the chart then the test was performed at 1m. A strict forced-choice testing procedure was used. The subject had to read the letters, even if they appeared illegible, until four or five letters on a row were named incorrectly. Visual acuity was scored as the total number of letters read correctly and converted to $\log_{10}$ minimum angle of resolution (log MAR) (Bailey et al. 1991).

For this study distance visual acuity was measured binocularly and monocularly, in random order, for each eye with the patient's best refractive correction.

5.2.2 Reading acuity test

The MNRead acuity charts (Legge et al. 1989) were used to measure reading acuity. They were developed at the Minnesota Laboratory for Low Vision Research at the University of Minnesota in the U.S.A. They contain sentences with 19 different print sizes. Each sentence is 0.1 log MAR units smaller than the previous sentence. From the recommended viewing distance of 40 cm the print size ranges from 1.3 to –0.5 logMAR. This range can be extended by

using a shorter or longer viewing distance. The MNRead chart has been carefully calibrated to give correct logMAR sizes, which are printed beside each sentence. Reading acuity is determined by the smallest print size at which the patient can read the entire sentence without making significant errors.

For this study reading acuity was measured at 25cm distance with the patient wearing an additional +4.00 DS over his distance correction. Both monocular and binocular reading acuities were recorded in log MAR units using the formula provided by the manufacturer: acuity=1.4- (sentences x 0.1) + (errors x 0.01), where sentences are the number of sentences read correctly and errors are the number of words read incorrectly. The calculated value was adjusted for this distance by adding to the measured acuity a +0.204 log MAR correction.

5.2.3 Contrast sensitivity test

Contrast sensitivity was measured using the Pelli-Robson letter sensitivity chart (Pelli et al. 1988). It consists of eight rows of six uppercase Sloan letters. The letters are arranged in groups of three. They are of a constant size (20/640 Snellen equivalent) but their contrast is decreased between the groups by 0.15 log units. Contrast sensitivity is scored letter by letter (Elliott et al. 1991) until two or three of the letters in the group are named incorrectly by the patient. Contrast sensitivity is recorded as log contrast sensitivity ($\log_{10}$ 1/contrast of letters at the threshold of visibility). The test was performed at 1m distance under controlled room illumination (approximately 100cd/m^2) with the patient wearing best corrective refraction for distance. No additional correction was used. According to the manufacturer's instructions an addition of +0.75 diopters for the 1 meter distance is only optional as the patient's sensitivity is unaffected by small refractive errors because the letters are at 1-1.6 cycle per degree at 1 metre (Pelli et al 1988 and 1991).

Although this test produces only a single measure of contrast sensitivity (peak contrast sensitivity) it has been reported that such measurement is most closely related to visual tasks such as reading (Rubin and Legge 1989) and face recognition (Owsley and Sloane 1987). These tasks are severely impaired in AMD patients and the effect of contrast on subjects' performance can be reliably predicted by this test (Rubin and Legge 1985; Peli 1986). For this study

both monocular and binocular contrast sensitivity were recorded in random order.

5.3 ASSESSMENT OF BINOCULAR FUNCTION

5.3.1 Cover test

Observation alone is not always sufficient to determine a manifest deviation of the visual axes (heterotropia). Covering one eye of a patient with normal binocular vision interrupts fusion. During this test the patient initially is asked to fixate with both eyes on a target such as a figure pasted on a tongue depressor or a 6/9 visual acuity symbol, while a cover is placed in front of one eye (von Noorden and Campos 2002). The fellow eye is observed for any potential movement. If there is heterotropia then the fellow eye will move to take up fixation.

For this study the cover test was used to investigate the possibility of the patient using a different retinal locus to fixate the target when viewing with both eyes versus one eye. The subjects were asked to fixate the centre of a target at 33cm distance with both eyes. The target was a ~4° black dot with a central white opening of ~1° (large enough to be visible by all patients) mounted on a plastic ruler. Then, one eye was covered with an occluder and any observed movement of the fellow eye indicating the take up of fixation was recorded (upward, downward, inward or outward movement). The same procedure was repeated for both eyes until the examiner was confident that the patient's response was reliable.

5.3.2 Device for assessment of binocular fusion

To test for simultaneous binocular perception the Bagolini striated glasses were used. They consist of plano glass lenses marked with fine, parallel striations. The mounted lenses were placed in a trial frame with the striations at an angle of 135° for one eye and 45° for the other eye. A line image of a small light source is produced at 90° to the striations, while allowing the patient to see the light through the lenses. In normal subjects the two lines will intersect at the

point of the light forming a cross. If binocular fusion is disrupted only one line will be perceived (Bagolini 1985). A light of a pen torch was used as the fixating stimulus. The patient was asked to fixate with both eyes at the light source and report if he could see one line or a cross. Optical correction was worn during the test. The test can be used at 6m, 33cm or in any desired distance. Such glasses have been routinely used in the analysis of suppression or anomalous retinal correspondence in patients with ocular deviations. However, it has been suggested that in patients with macular disease the stimulus can still be perceived using eccentric viewing and a cross can be seen. However, gaps in the perceived lines have been reported (von Noorden and Campos 2002).

For this project by using the Bagolini glasses we tested our subjects for evidence of simultaneous binocular perception by using a "full field" streak. We used the grade No4 Bagolini lens with thicker striations in order to produce streaks visible to our low vision patients. We performed the test at 33cm distance and the patients wore a spectacle correction for this distance (+3.00 dioptres in addition to the distance correction). Initially, the patient had to see the streak by each eye under monocular viewing conditions and afterwards he had to indicate if he could see a cross or a line under binocular viewing conditions. If only one line was seen, then the direction of the line and any perceived gaps across the line were documented. If there was no perception of gap in the perceived line despite existing retinal scotomas, a filling-in mechanism within the scotomatous area was assumed (Zur and Ullman 2003).

5.3.3 Device for assessment of binocular fusion at and near the PRL area

To assess binocular fusion at the area of the preferred retinal locus the CrystalEyes glasses were used (Figure 5.1).

Figure 5.1. CrystalEyes glasses system

This system includes a set of eyewear with a pair of liquid crystal shutters. The shutters can be electronically controlled to either pass the light through or to block all light from passing through. It also contains an infrared emitter that connects to the user's workstation, which sends out a pulse and selectively activates the shutters in synchronization with the left or right image sequence on the display screen, allowing only the correct images to reach each eye. Field rate can vary from 80 to 160 fields per second. Each eye of the subject, when wearing the eyewear, will see for example 80 fields of image per second, out of phase with the other 80 fields shown to the other eye. The subject sees a fused image. The field of view with the eyewear is 90° vertically and 140° horizontally.

In contrast to Bagolini glasses, where the overall simultaneous binocular perception was tested, the CrystalEyes glasses were used to test simultaneous binocular perception at a more localised area, such as their PRL, and also at the immediate visual field area outside the macular scotomas.

The subject was seated 50 cm away from the computer monitor (21" Trinitron GDM-F500R, Sony, Japan) during the test and wore a spectacle correction for this distance (+2.00 dioptres in addition to the distance correction). The background screen luminance was 125cd/m^2, screen resolution was 1024x768 pixels and the refresh rate was 70 Hz, therefore, field rate was 140 fields per second. The size (height and width) of the targets used (lines and letters) were adjusted to patient's distance visual acuity (3 ×threshold of distance log MAR acuity). This size was selected as the minimum acuity reserve reported for "high fluency" reading in macular disease patients is 3:1 (Whittaker et al. 1991; Lovie-Kitchin et al. 2000) in order the targets to be visible to the patients. Initially, the patient had to see the line or the letters by each eye under monocular viewing conditions and afterwards he had to indicate if he could see a cross or a line and read the letters under binocular viewing conditions. If only one line was seen, then the direction of the line was documented. The number of letters seen was also recorded.

The test was divided in two parts. During the first part by using the CrystalEyes glasses one black line was presented at 45° to one eye and a second black line

was presented at the opposite direction (135°) to the other eye. Both lines were centrally displayed on the computer monitor. The patient had to report his perception of this image and his response was documented as seeing a cross or one line (its direction was also recorded). Patients who use retinal areas for binocular fixation outside their scotomas and retain normal fusion at their PRL should report the perception of a black cross. In the second part five letters were presented to the patient. The central letter was projected to both eyes, while two of them were projected to the right eye and two to the left eye. The patient was asked to read the letters during four trials. Patients with normal fusion should read correctly all the letters that fall outside their scotomatous areas.

During both parts of the test patient's vergence was monitored by diagonal lines that were placed at the four corners of the monitor all pointing at the central target.

5.3.4 Stereoacuity test

In order to test stereoacuity levels in patients with bilateral AMD the Frisby test was used (Frisby et al. 1975). Although there are several tests for measuring stereoacuity, such as the TNO-test, Lang stereo test etc., the main reason for selecting the Frisby test was the fact that good visual acuity is not essential to perform the test. This test consists of three transparent, plastic plates of different thickness (6, 3 and 1mm), which permit a large range of stereoacuity measurements (600 to 15 seconds of arc). Each plate consists of four squares of small curved random shapes. One square contains a 'hidden' circle, which is printed on the back surface of the plate. The patient has to decide in which pattern the hidden shape lays starting from the thickest plate, progressing to the thinner plates, if the response is correct. The test is three-dimensional and does not require polarised or coloured spectacles. The task can be successfully done only if stereopsis is present. The disparity is created by the thickness of the plate and can be changed by increasing or decreasing the viewing distance.

For this project the test was performed initially at 30 cm with the 6mm plate, then with the 3mm and then with the 1mm plate. If the patient was successful

the test was performed at 40 cm distance with all the plates, then at 50 cm, 60 cm, 70 cm and finally at 80 cm.

5.4 IMAGING TECHNIQUES AND FUNCTIONAL EVALUATION OF THE POSTERIOR POLE

5.4.1 Scanning Laser Ophthalmoscope (SLO)

New imaging techniques developed over the last two decades allow a wide range of new possibilities to visualize the retina in vivo. Scanning Laser Ophthalmoscopy was introduced by Webb and co-workers in 1980 and has been used successfully for many scientific and clinical purposes (Webb et al. 1987). Today, Scanning Laser Ophthalmoscopes (SLOs) provide facilities for confocal imaging of the retina (e.g. reflectance imaging, fundus autofluorescence imaging) (von Ruckmann et al. 1995; Bellmann et al. 1997) , fluorescein and indocyanine green (ICG) angiography (Bartsch et al. 1995; Dithmar et al. 1997 ; Holz et al. 1998), and psychophysical measurements such as microperimetry, fixation and reading tests (Timberlake et al. 1986; Culham et al. 1992; Sunness et al. 1995; Fletcher and Schuchard 1997; Lei and Schuchard 1997; Rohrschneider et al. 1998; Fletcher et al. 1999).

The principal difference between conventional ophthalmoscopy and confocal scanning laser ophthalmoscopy is the method of illuminating the retina. In scanning laser ophthalmoscopy, a laser beam scans across the retina. Since the entire light energy is focused onto a small spot for only a short period of time, much less light is necessary to illuminate the retina. Afterwards, the reflected or emitted light goes the same way back through the optics, separated from the incident laser beam, and deflected to a detector.

In addition to low light level illumination, confocal scanning laser ophthalmoscopy allows imaging through small pupils and reduced media. Confocal imaging is possible by introducing a pinhole aperture in the optical pathway. This means that structures above or below the depth of interest are suppressed resulting in higher image contrast in the area of interest. Although other forms of scanning laser ophthalmoscopy such as optic nerve head

tomography and optical coherence tomography are the more widely used techniques today retinal imaging and psychophysical testing using SLOs are still of great interest.

For our project we used the Rodenstock device (today Rodenstock, Weco, Düsseldorf, Germany- Model SLO-101) (Figure 5.2).

Figure 5.2. Scanning Laser Ophthalmoscope (Rodenstock, Model SLO-101).

This device contains three different lasers (Argon laser with a 488nm and 514nm wavelength, HeNe-laser with 633nm and infrared diode laser with a 780nm wavelength). The screen subtends 20° or 40° diagonal and this means for the latter one a fundus image size of 33°x21°. The whole image has a resolution of 786 by 576 pixels. The optics of the instrument allows spherical error compensation between –20 and +20 diopters.

Scanning Laser Ophthalmoscope Microperimetry

The Rodenstock SLO has the advantage of additional facilities for psychophysical measurements such as microperimetry and fixation tests. Visual test stimuli are produced with the HeNe-laser and projected directly on the patient's retina. The stimuli can be modulated over a range of 0 dB to 31 dB (approximately 3 log units steps of intensity). The size of the fixation stimulus is changeable between 24x24 min arc and 750 x 750 min arc. Since the examiner is able to get a real time image on the monitor, it is possible to determine the retinal location of the visual stimuli and to produce an accurate documentation of the relationship between visual function and retinal pathology.

For this study we used the SLO to identify the monocular PRL for each eye and to map macular scotomas.

5.5 EYE MOVEMENT RECORDING SYSTEM

5.5.1 Eye tracker

Many devices have been previously used to monitor eye movements such as fundus cameras (White and Bedell 1990; Nilsson et al. 1998), scleral search coils (Cummings et al. 1985) and infrared eye trackers (Bullimore and Bailey 1995). An infrared eyetracker (SMI EyeLink Gaze tracker, SensoMotoric Instruments, Teltow, Germany) was used for this study (Figure 5.3).

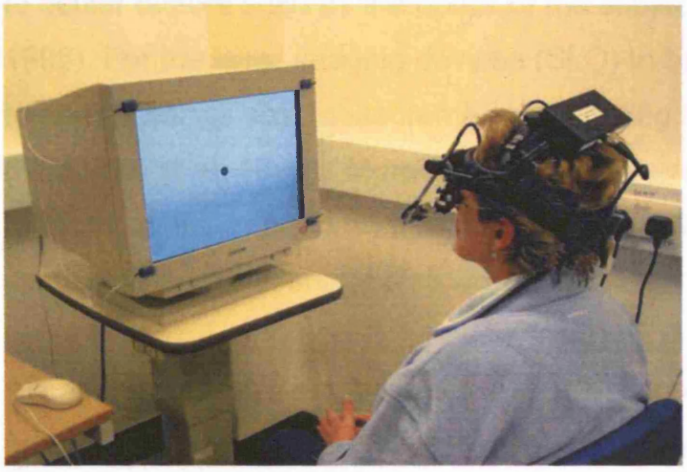


Figure 5.3. SMI EyeLink Gaze tracker.

It consists of two infra-red cameras that image the pupils, while a third camera monitors the position of the subject's head relative to four IR markers mounted on the display screen. The cameras are mounted on a headband which is adjustable to the patient's head so recording of eye movements can take place allowing free movement of the head which has the advantage of more natural recording conditions. The device compensates for head movements so the actual position of gaze can be calculated with precision. This eye tracker has gaze position accuracy of <0.5°, while eye position is sampled at a rate of 250 Hz. Gaze position tracking range is estimated ≥ +/- 20° horizontally and +/- 17° vertically with moderate head motion. Calibration, drift correction and validation are performed using manufacturer's algorithms.

For this study, eye movements were recorded monocularly and binocularly in random order to investigate monocular versus binocular viewing for fixation tasks and reading performance in AMD patients.

5.6 CROSS CALIBRATION TECHNIQUES BETWEEN THE EYETRACKER AND THE SLO

It has been reported that the image size using fundus imaging systems depends mainly on the magnification due to the camera and magnification due to ocular factors such as the optics of the subject's eye (Garway-Heath et al. 1998). For the laser imaging devices (SLO) in-built correction factors are used to correct image size measurements according to the patient's refractive error (Rudnicka et al. 1998). Moreover, refractive errors from all of our patients were relatively small (ranged from emmetropia to -4.00 diopters and therefore, only small differences in image size were expected.

According to the main project's protocol two different devices were used to record patient's fixation locus under monocular (eyetracker and SLO) and binocular viewing (eyetracker). Therefore, it was important to match the background luminance and stimulus intensity used during testing with these devices (the SMI eye tracker uses a PC monitor, while the SLO has its own screen) and the magnification of these two systems.

5.6.1. Matching the magnification

In order to calibrate the magnification factor for the pixel size used in these instruments a simple experiment was designed. Five crosses were projected on the SLO monitor using the He-Ne laser beam (He-Ne power used was 3μw and infrared 100μw). One cross was centrally located and the other four were positioned on the four corners of a 40° field. The crosses measured 100 pixels vertically and horizontally. The SLO was positioned at a right angle to the wall from a distance of 167cm. A beam splitter was attached to the SLO and positioned at 45° angle in order to project by reflection the five crosses from the SLO to a white paper mounted on the wall. Subsequently, we marked the borders of the SLO crosses on the paper and we measured them in cm.

The crosses varied from 13.6 to 15cm vertically and from 12.2 to 13.2cm horizontally. The variation was less than 10% in both directions. The central cross was 13cm horizontally and vertically. No consistent difference in size was noticed for the crosses located at the periphery of the SLO field. The distance from the wall to the beam splitter was 167cm and from the beam splitter to the front part of the eye (measured from the most anterior part of the cornea) was 4cm. Given a total distance from the eye to the wall was 171cm and a cross height of 100 pixels, we determined that: *1 pixel =2.6112 min of arc or 1°=22.9 pixels.*

For the PC monitor we made similar calculations. Our PC monitor had 1024 pixels horizontally and its screen measured 39.5 cm, so we concluded that:
1 pixel=2.638 min of arc or 1°=22.7 pixels.

In summary, the angular subtense of the pixels for the SLO and the eyetracker were similar. We used 1°=23 pixels for the rest of the project in order to describe our results in degrees of visual angle for both instruments.

5.6.2. Matching the luminance

To match the background luminance and stimulus intensity used during testing with the two devices (PC monitor used during recordings with the eyetracker and the SLO) the luminance of the SLO was calculated by Mr Glen Harding based on the method described by Nygaard (Nygaard and Schuchard 2001). In brief, luminance from different luminous surfaces (human faces, newspaper, TV screen etc) was measured in cd/m^2 using a hand held radiometer. The measured luminance was referred as a 'free source luminance' and it was defined as the brightness of everyday objects. Consequently, using an algorithm described in the paper luminance converted to SLO power values in μW (Figure 5.4).

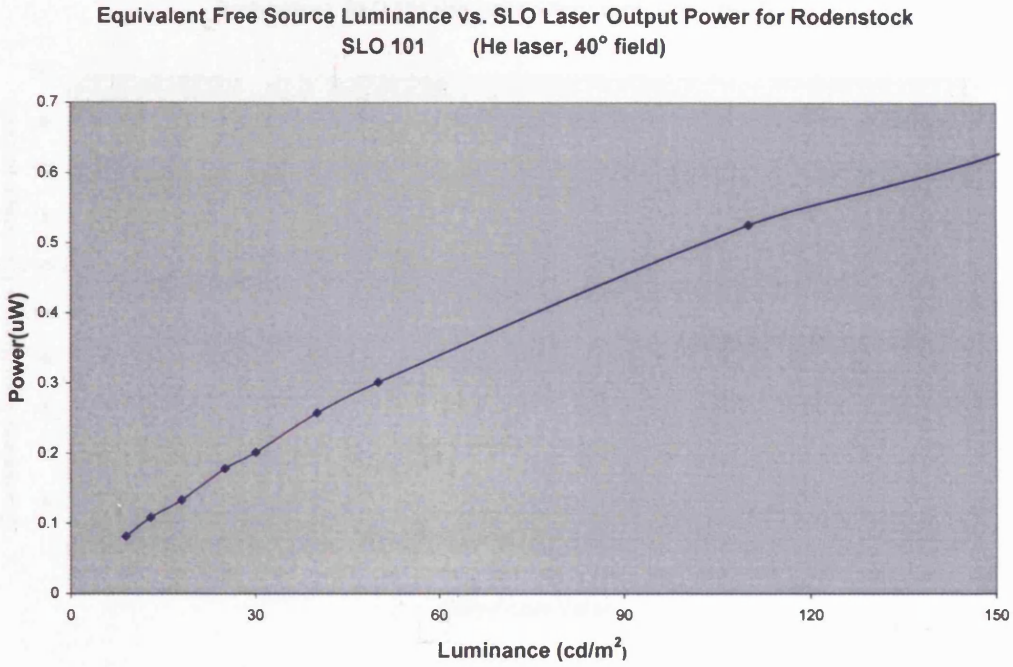


Figure 5.4 Free source luminance in cd/m² was inserted in the formula described by Nygaard et al. and the SLO output power was calculated in µW (Rodenstock SLO, He Ne laser power level 3; field of view 40°).

Subsequently, by using different grey scale values on the SLO, the output laser power was measured in µW. Combining the latter and the graph in figure 5.4 a new graph was constructed, where grey- scale values were translated in equivalent free source luminance values for the Rodenstock SLO (Figure 5.5).

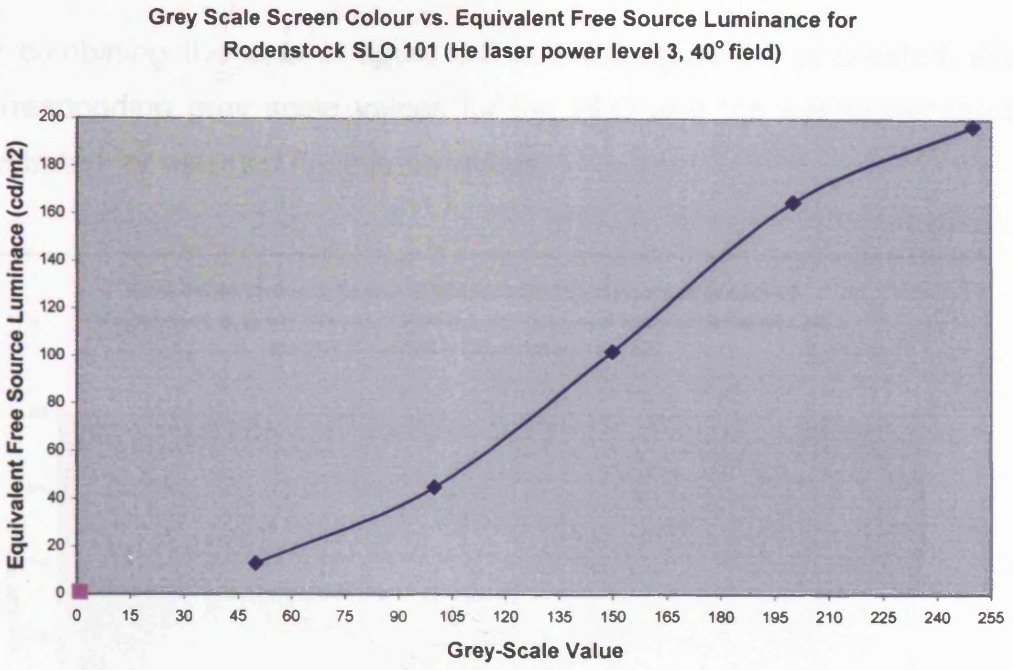


Figure 5.5 The equivalent free source luminance was calculated based on different grey-scale values from the Rodenstock SLO, when the He Ne laser power level was 3 and a 40° field of view was used.

The luminance of the PC monitor used during eyetracker recordings was also calculated using a chromometer (Minolta CS-100) and is plotted in figure 5.6.

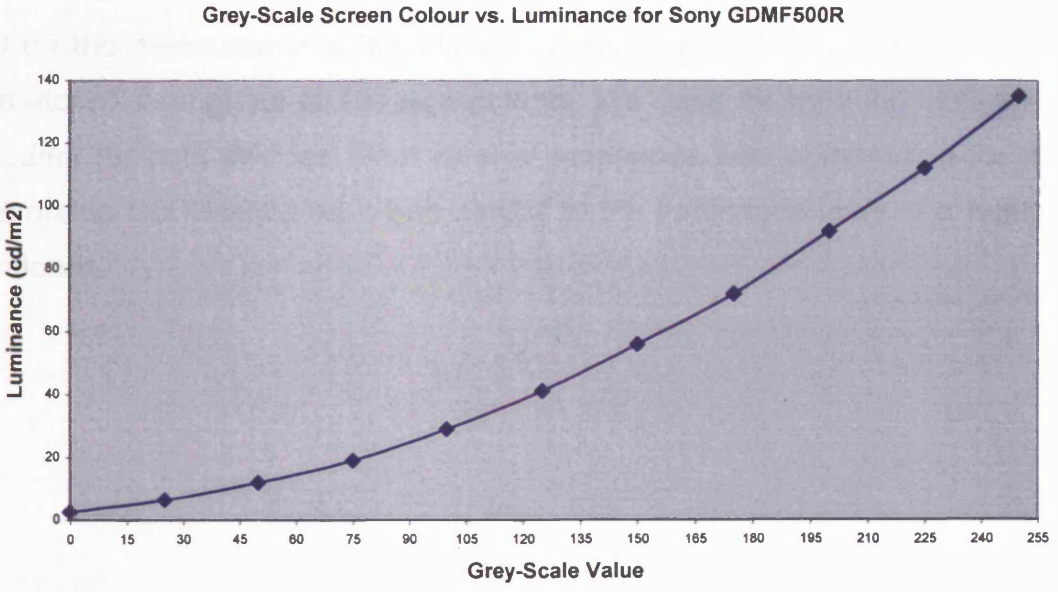


Figure 5.6. Free source luminance was calculated based on different grey-scale values from the PC monitor of the eyetracker system.

By combining the data in figure 5.5 and 5.6 figure 5.7 is created, where the corresponding grey scale values for the SLO and the eyetracker monitor are illustrated for selected luminance values.

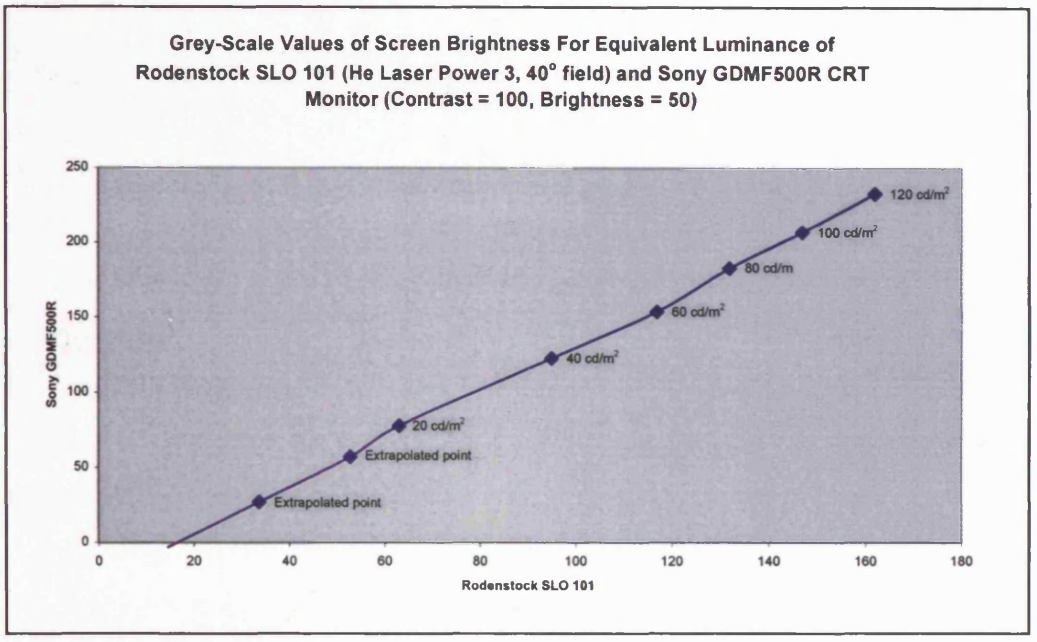


Figure 5.7 Grey-Scale values of screen brightness of the Sony GDMF500R CRT Monitor (Contrast = 100, Brightness = 50) are plotted against Equivalent Luminance of Rodenstock SLO 101 (He Laser Power 3, 40° field of view).

Based on the measurements, luminance in both the SLO and the eyetracker were matched throughout all the experiments. We used background luminance ~ 125cd/m^2 for both devices. That level of luminance was comfortable for the patient during SLO testing as it was similar to the luminance level of a human face indoors.

CHAPTER 6

6.1. MAPPING OF THE PHYSIOLOGICAL BLIND SPOT: A VALIDATION STUDY

6.1.1. General concept

One of the main purposes of the thesis was to explore binocular versus monocular viewing in AMD patients and more specifically the PRLs used under the two conditions. As was described earlier, due to the unavailability of an instrument which provides all of this information, the combined use of two different devices was required to collect our data; the eyetracker for collection of monocular and binocular data of gaze position and the SLO for monocular recording and PRL identification on the retina. However, the eyetracker allows recording in natural viewing conditions (chapter 5.5), while the SLO operates at a fixed viewing distance and with a rigid head and chin support (chapter 5.4). Therefore, it was necessary to demonstrate that the data acquired using these two dissimilar instruments were comparable. Hence, we designed a task for measuring the horizontal and the vertical distance from the centre of the natural blind spot to the retinal locus used for fixation of a target. As the centre of the blind spot is always in the same place within a given observer in a given eye, the accuracy of estimating these distances by performing the same experiment using both the SLO and the eyetracker provide a useful calibration mark between the two devices. In addition, previous work has shown that these measurements (horizontal and vertical eccentricity of the centre of the blind spot) were relatively easy to map (see below).

The existence of the normal blind spot within the field of vision was first noted by Mariotte in 1668 (Carbajal 1957). Marriotte's physiological blind spot may be defined as 'a non-seeing area in the field of vision corresponding to the position and extent of the optic nerve head', an area that has no rods or cones. It is a vertical oval approximately 7.5° by 5.5°, with its centre located about 15.5° temporal to the point of fixation and about 1.5° below the horizontal meridian. Little interest was shown in the further study of the area until the beginning of the 19th century, when more reports started to appear in the literature in an

effort to describe and measure the blind spot parameters (Duke-Elder 1939; Chamlin 1960). Duke-Elder presented a summary of these recordings including findings as early as 1912 (Duke-Elder 1939). According to these data it seemed that the horizontal diameters varied from 4° to 6.5° while the vertical diameters varied from 3° to 8°. There are several factors affecting the size of the blind spot such as the subject's refractive error or intensity of illumination. Different techniques have been used to measure the blind spot in normal subjects or in patients using an ordinary tangent screen, automated perimetry (Rudnicka and Edgar 1995), fundus camera (Meyer and Howland 2001) or more sophisticated instruments such as SLOs (Garway-Heath and Hitchings 1999; Meyer and Howland 2001). Several attempts have also been made in the past to use the physiological blind spot as a marker for fixation using the SLO or simpler psychophysical methods (Hu SY 1994; Mackeben and Gofen 2001)

We designed a technique for mapping psychophysically the natural blind spot in collaboration with Dr Elisabeth Fine of Schepens Eye Research Institute, Boston, USA.

6.1.2. Purpose

The purpose of this study was to demonstrate that the data obtained using the SLO was comparable to the data from the eyetracker when measuring the distance from the centre of the blind spot to the normal fovea using these devices.

6.1.3. Methods

Ten young subjects, aged 20–35 years (group 1), and nine older individuals, aged 60–74 years (group 2), with normal vision and no known ocular pathology were included in the study. Subjects with refractive error >4 DS were excluded from this study. The test was performed monocularly (the subject chose which eye would be tested), while the fellow eye was occluded.

Eyetracker recordings

The subject was seated 50 cm away from the computer monitor (21" Trinitron GDM-F500R, Sony, Japan) during the test and wore a spectacle correction for

this distance (+2.00 dioptres in addition to the distance correction). The background screen luminance was 125cd/m^2, the screen resolution was 1024x768 pixels and the refresh rate was 70 Hz. Calibration of the instrument was performed using the manufacturer's algorithms before initiation of data recording. The characteristics of the stimuli used (fixation and mapping stimuli) are presented in table 6.1.

Table 6.1 Size, colour, stimulus and background intensities for both fixation and mapping stimulus.

Fixation Stimulus		Mapping stimulus
Size	1.7°	0.9°
Colour	Dark cross	Dark disc
Stimulus intensity	5.8 cd/m^2	5.8 cd/m^2

Mapping Procedure

The fixation target was first displayed on the computer monitor and the subject was instructed to sit as still as possible and maintain stable fixation on the target during the entire test. Fixation was monitored continuously with the eyetracker. Previous reports have demonstrated that the standard deviation of the position of a subject's line of sight on a single meridian while sitting is on the order of 15 min of arc. Physiological nystagmus, micro saccades and slow drifts account for the instability (Steinman et al. 1982). A value of ±2SD (1°) of the normal deviation of position of gaze was used as a control value for patient's fixation behaviour to ensure an accurate mapping of the blind spot. Therefore, if the subject's fixation deviated from the fixation target during the test by more than 1°, the trial was discarded.

The mapping stimulus was initially placed within the blind spot while the subject maintained fixation on the cross. This default starting position was chosen based on previous data on the distance between the centre of the normal blind spot and the fovea (15.5° temporal to the point of fixation and about 1.5° below the horizontal meridian) (Steinman et al. 1982). Subsequently, the investigator moved the stimulus from a not seen (within the blind spot) to a seen point

(outside the blind spot). When the moving stimulus was detected by the observer he reported it to the examiner and the position of the target was recorded. Movements in each of four cardinal directions were tested in random order. Three practice runs were followed by six test runs. The experiment for each subject was performed twice in order to test repeatability of the procedure.

SLO recordings

The subject was seated against the SLO without his spectacles and his distance correction was added to the SLO. The stimuli, the mapping procedure and the background luminance used were identical to the eyetracker recordings. The test was also performed twice to test its repeatability.

Data analysis

Recorded data were used to calculate the x- and y - coordinates of centre of the blind spot from fixation (horizontal distance and vertical distance accordingly). Data were averaged over six runs for each subject for each mapping condition. An overall mean and SD was calculated for each condition to determine the normal variation in the centre of the blind spot parameters for both groups (young and older group). Measurements were compared for each subject across both mapping conditions. The repeatability of all procedures was also evaluated. The performance of old and young subjects was compared for each device.

6.1.4. Results

The SAS/JMP statistical package (SAS Institute, version 5.1a) was used to analyse the results. The mean and SD of the horizontal distance and vertical distance of the centre of the blind spot from fixation for both groups (young and older group) and for each experimental technique are presented below in table 6.2. Repeated measures ANOVA was used to evaluate differences in the horizontal and vertical eccentricity of the blind spot centre from fixation for both groups using the two devices. The p-values for the measurements are also given below. The differences are not statistically significant at the $p<0.05$ level for any of the groups, as shown in table 6.2.

Table 6.2 Mean horizontal and vertical eccentricity and SD of the blind spot centre with respect to fixation for the normal young and the older group and for both devices (SLO and SMI) in degrees of visual angle. P values for between the two age groups (between subjects analysis) and the two devices (within subjects analysis) are also presented.

	SLO	EYETRACKER	
HORIZONTAL ECCENTRICITY			
Old group	16.4° ± 1.5°	16.5° ± 1.5°	*p=0.91 (between the two age groups)*
Young group	16.7° ± 0.8°	16.3° ± 0.9°	
	p=0.53 (between the two devices)		
VERTICAL ECCENTRICITY			
Old group	2.0° ± 0.5°	2.1° ± 0.4°	*p=0.63 (between the two age groups)*
Young group	2.0° ± 0.7°	1.7° ± 1.0°	
	p=0.54 (between the two devices)		

The horizontal and vertical eccentricity of the blind spots' centre mapped with the SLO and the eyetracker for both groups are described in figure 6.1.

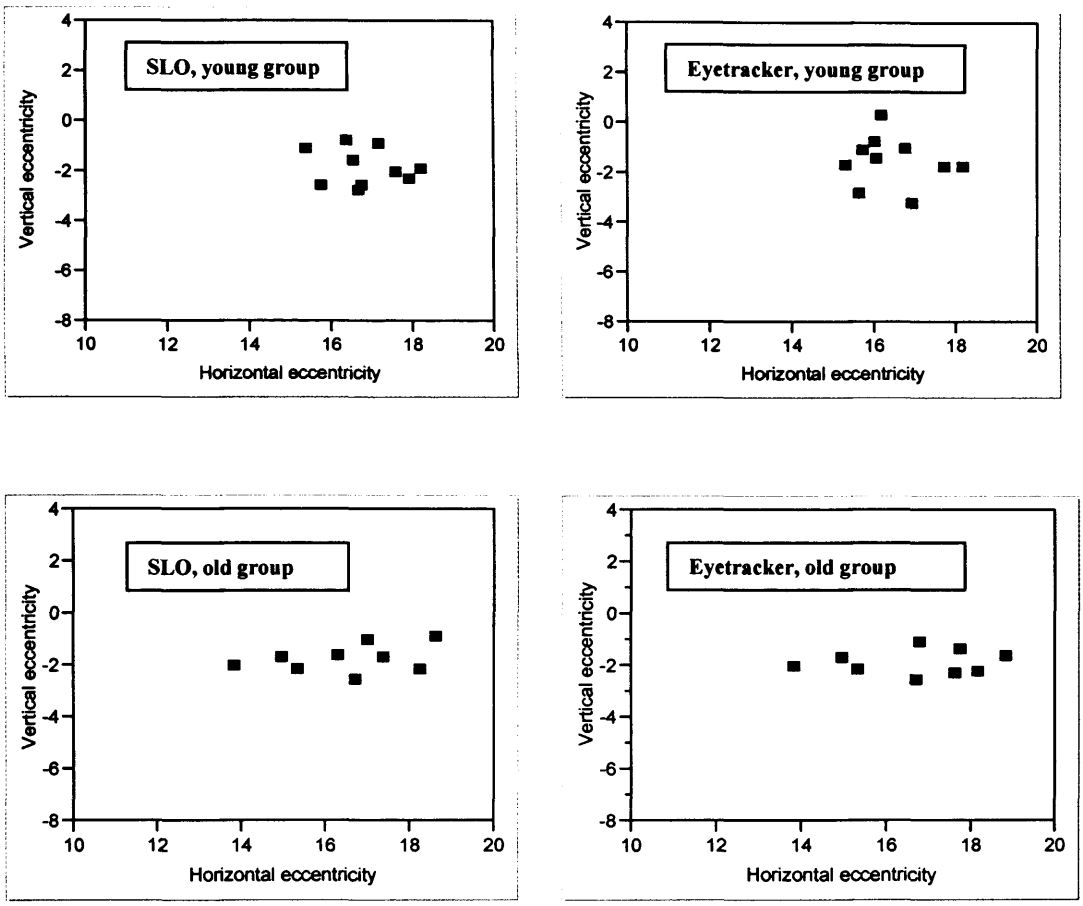


Figure 6.1. Horizontal and vertical eccentricity of the blind spots' centre from fixation mapped with the SLO (top left) and the eyetracker (top right) for group 1 (young group) and with the SLO (bottom left) and the eyetracker (bottom right) for group 2 (older group). The 0,0 point corresponds to the centre of fixation (fovea in normal subjects). Minus signs in the vertical axis represents the lower visual field (below fixation) and positive signs represent the upper visual field (above fixation).

The distances between the centre of the blind spot and fixation as measured with the two devices are superimposed on the SLO image of one young subject, which was a representative example of the accuracy of the technique using the two different instruments (figure 6.2). Both distances were centred at the centre of the blind spot calculated from the SLO data.

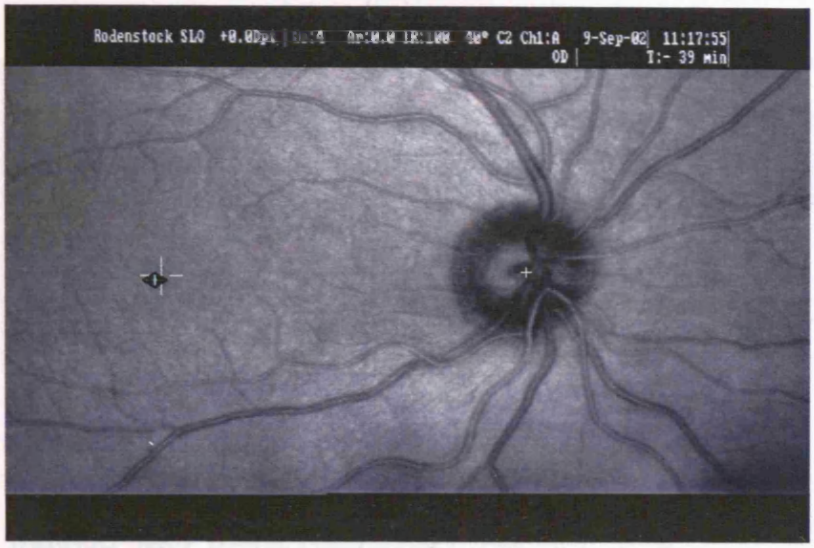


Figure 6.2.The distances between the centre of the blind spot and fixation as measured with the SLO and the eyetracker superimposed on the SLO image of one young normal-sighted subject. The large white cross represents the location of the subject's fixation during the SLO recording and the blue cross the fixation during testing with the eyetracker. The small white cross represents the centre of the blind spot for this subject. Note the close relationship of the two fixation crosses.

Repeatability

Two consecutive measurements were performed by 10 young and 4 older subjects to measure the repeatability of the procedure using both devices. The mean of the difference between the first and second recording and the 95% C.L. were calculated for both instruments and for both groups (Bland and Altman 1986). The results of this analysis are presented in table 6.3. In summary, the data acquired from the two methods differed less than 0.42° in both groups, while the difference between the two groups for both devices was not more than 0.3°.

Table 6.3 Mean of the difference between the first and second recording and the 95% C.L. for both instruments and for both groups. H= horizontal eccentricity, V= vertical eccentricity.

	Young Group				Old Group			
	SLO		Eyetracker		SLO		Eyetracker	
	Mean	95% CL	Mean	95% CL	Mean	95% CL	Mean	95% CL
H	0.07	-0.30→ 0.16	0.49	-1.08→ 0.13	0.37	-3.00→ 2.25	0.42	-3.01→ 2.15
V	0.16	-0.19→ 0.52	0.20	-0.16→ 0.56	0.20	-0.76→ 0.35	0.10	-0.66→ 0.04

The coefficient of repeatability were also calculated in order to determine if one method was more repeatable than the other and whether the young group provided more repeatable results than the old group. The results are presented in table 6.4.

Table 6.4 Coefficient of repeatability between the first and second recording for both instruments and for both groups. H= horizontal eccentricity, V= vertical eccentricity.

	Young Group		Old Group	
	SLO	Eyetracker	SLO	Eyetracker
H	0.48	3.0	1.50	1.70
V	1.05	1.27	0.80	0.40

It is evident that the SLO results were more repeatable than the SMI data for both groups except for the vertical eccentricity of the blind spot as measured with the SMI. Moreover, results were more repeatable for both instruments in the old group compared to the young group, except from the horizontal eccentricity which showed higher repeatability in the young group.

6.1.5. AMD data

We attempted to use similar methods to measure the distance between the centre of the blind spot and the PRL using both devices in AMD patients in order to demonstrate that data were comparable between the two devices. Initially, six patients with bilateral AMD were recruited. However, data were acquired on both instruments only in one patient as three patients managed to perform the test using the SLO only, while two of them failed to do the test in

both devices. It appeared that the test was too demanding to be performed by AMD patients. The main problem for the test using the eyetracker was the complexity of predicting the starting position of the mapping stimulus as these patients were using a PRL instead of their normal fovea and there was no default starting position to guide us. In addition, AMD patients had great difficulty keeping their fixation stable, while paying attention to the more peripherally presented mapping stimulus. Therefore, recording time was very prolonged and tiring for the patient, which led to incomplete testing. Unpublished data from other researchers in our lab supported our hypothesis that AMD patients have difficulties dividing their attention efficiently between their PRL and another peripheral locus simultaneously. On the contrary, normal sighted subjects, both young and older subjects, can successfully fixate a target with their fovea, while attending to another target with a peripheral retinal locus.

Data acquired from the above AMD patient is presented below. This patient had bilateral AMD and log MAR distance visual acuity 0.3 in the right eye and 1.0 in the left eye. We managed to get recordings only from his better right eye. An infrared SLO picture of his right central retina with the calculated horizontal and vertical distance between the blind spot centre and his fixation locus is presented in figure 6.3. The horizontal eccentricity of the centre of the blind spot with respect to his PRL was measured at 16.8° for the SLO and 15.8° for the eyetracker and the vertical distance was measured at 3.5° for the SLO and 2.2° for the SMI.

Figure 6.3. SLO infrared image of the right fundus of one AMD patient. SLO and eyetracker recordings during mapping of the centre of the blind spot in respect to the fixation locus have been superimposed on this image. The pink cross represented the fixation locus as recorded using the eyetracker while the blue cross represented the fixation locus as recorded using the SLO. The centre of the blind spot was marked with a red cross. The different colour circles around the blind spot outline the psychophysical borders of the blind spot using the different devices (pink circle = eyetracker, blue circle = SLO).

It should be noted that there was a close relationship in the PRL positions measured with the two devices. Although there was a larger difference in the vertical eccentricity, the difference between the horizontally eccentricity as measured by the two devices fell well within their test-retest variability. This indicates that data acquired with the two devices were comparable. Furthermore, these results suggest that the patient was using the same retinal locus to fixate while performing the task using the SLO and the eyetracker. Unfortunately more data could not be collected in order to draw more general conclusions regarding patients' fixation behaviour and therefore the test was abandoned.

6.2. PREDICTION OF BLIND SPOT CENTRE BASED ON SLO PICTURES

According to the results presented previously, it was not feasible to locate the centre of the blind spot and measure its distance from the PRL for most AMD

subjects with the psychophysical mapping technique. As it was important for this project to accurately identify the centre of the blind spot on the SLO images we investigated how accurate was the prediction of the centre of the blind spot by just examining the infrared SLO images and locating the centre manually.

6.2.1. Methods

Nine infrared SLO images of normal subjects included in the previous study were examined by the investigator. The centre of the blind spot was marked manually for each image. Their x- and y- coordinates (predicted values) were then compared with the calculated values on the same subjects during the physiological mapping of the blind spot using the SLO.

6.2.2. Results

The mean of the difference in horizontal eccentricity between the predicted and the calculated values was 0.02° (95% C.L.= -0.37° - 0.15°). For the vertical eccentricity the mean of the difference between the two measurements was 0.06° (95% C.L.= -0.24° - 0.37°). As the differences were very small we considered that we could predict the centre of the blind spot accurately by examining SLO images.

The results of this study are used later (chapter 8) to calculate the centre of the blind spot in AMD patients in order to predict the retinal locus of the normal fovea before the onset of the disease.

6.3 CONCLUSION

The centre of the blind spot can be accurately mapped with respect to fixation by means of an SLO and an eye tracker using the technique described above in normal individuals. There were no systematic differences between young and old observers or between the two devices for any of the blind spot parameters measured. The results were repeatable for both instruments. Our results demonstrated that data acquired with both devices were comparable and therefore, the SLO and the eyetracker can be used accurately in cross calibration measurements.

Our data regarding the distance between the centre of the blind spot to normal fixation using different devices and measured in different age groups (16.7° ± 0.8° horizontal eccentricity and 2.0° ± 0.7° vertical eccentricity for the SLO and 16.3° ± 0.9° horizontal eccentricity and 1.7° ± 1.0° vertical eccentricity for the eyetracker for the young group; 16.4° ± 1.5° horizontal eccentricity and 2.0° ± 0.5° vertical eccentricity for the SLO and 16.5° ± 1.5° horizontal eccentricity and 2.1° ± 0.4° vertical eccentricity for the eyetracker for the old group) were comparable with previously presented results (15.5° horizontal eccentricity and 1.5° vertical eccentricity from the point of fixation) (Duke-Elder 1939; Carbajal 1957). By using a similar psychophysical method Mackeben et al. demonstrated very similar results with a mean horizontal eccentricity of the centre of the blind spot of 14.8° (range 12.8°-17.1°) and a mean vertical eccentricity of 1.1° (range 0.1°-2.6°) (Mackeben M 2001). Using an SLO Hu et al. reported a mean horizontal eccentricity of 14.7° (range 13.2°-17.7°) and a mean vertical eccentricity of 1.9° (range 0.4°-3.1°) (Hu SY 1994).

However, AMD data were difficult to obtain when the disease was advanced and the patient was using an eccentric retinal locus to fixate instead of his normal fovea. Consistent with similar observations by other investigators in our lab, we found that AMD patients could not efficiently divide their attention by fixating a target with their PRL and simultaneously paying attention to another peripheral stimulus. Although we could test AMD patients with smaller scotomas in order to acquire more data, we felt that our results wouldn't be representative of AMD patients. Therefore, we used the same assumption that other studies have used previously (Schuchard et al. 1995; Crossland and Rubin 2002; Schuchard et al. 2003), that AMD patients are using the same PRL to perform a task on the SLO and other devices such as the eyetracker (Crossland and Rubin 2002).

The use of multiple PRL has been reported in the literature mainly in patients with newly acquired disease (Crossland et al. 2004a) and in cases where the experimental conditions were changing (Lei and Schuchard 1997). In order to control the latter factor we carefully matched the experimental conditions when using the two devices. In addition, subsequent analysis of fixation behaviour during eyetracker testing for our patients (see chapter 9) showed that all of

them, apart from one, were using a single PRL to fixate the target. This fact supports further the hypothesis that AMD patients are likely to use the same PRL during the same simple fixation task when using the SLO and the eyetracker, as it is less likely for the patient to use multiple or different PRLs during the same task on the SLO since there is less freedom there for head or eye movements.

Nevertheless, our measurements also showed that the centre of blind spot could be accurately located by evaluating SLO pictures through observation only. This information will prove useful in order to locate the blind spot centre and subsequently the locus of the former fovea in AMD patients with central scotomas (see chapter 8).

CHAPTER 7

ASSESSMENT OF VISUAL FUNCTION

Subjects

Thirty patients with bilateral AMD were included in the study. The mean age of AMD subjects was 79.8 years ± 5.6 SD. Biomicroscopic fundoscopy was performed and retinal appearance was documented for all patients in table 7.a in appendix 2.

7.1 CLINICAL VISION TESTS

7.1.1 Methods

Binocular and monocular distance and reading acuity and contrast sensitivity were recorded for all AMD subjects using standard clinical tests discussed in the general methods and instrumentation chapter (chapter 5.2.1, 5.2.2 and 5.2.3).

7.1.2 Results

7.1.2.1. Clinical measurements

The results of these tests are presented in detail in table 7.b in appendix 2. Overall, the mean values for the clinical tests in the AMD group were: mean 0.86 log MAR ± 0.3 SD for distance acuity (range 0.3-1.3), mean 1.01 log MAR ± 0.35 SD for reading acuity (range 0.35-1.51) and mean 0.86 log units ± 0.40 SD (range 0.0-1.35) for contrast sensitivity. The ranges and the mean values of the measurements for the better seeing eye, the worse seeing eye and binocular viewing are summarised in table 7.1. The better seeing eye was defined as the eye with the better distance acuity. If both eyes had equal distance acuity the eye with the better contrast sensitivity was characterised as the 'better' eye. There was a significant difference in acuities (distance and near) and contrast sensitivity between the better and the worse eye (paired t-test, $p<0.0001$).

Table 7.1. Range, mean and SD of the better, worse eye and binocular distance and reading acuity and contrast sensitivity for all AMD subjects. The results from paired t test analyses for these measurements for the better and worse eye are presented in the last column.

	Better Eye	**Worse Eye**	**Binocularly**	*Paired t-test (better versus worse eye)*
Visual acuity (logMAR)				
(range)	0.30 -1.06	0.80 -1.30	0.30 -1.04	Mean difference = 0.40;
(mean ± SD)	0.66 ± 0.28	1.06 ± 0.14	0.65 ± 0.28	p<0.0001
MNREAD acuity (logMAR)				
(range)	0.35 -1.24	0.72 -1.51	0.30 -1.34	Mean difference =0.52;
(mean ± SD)	0.76 ± 0.27	1.26 ± 0.21	0.75 ± 0.28	p<0.0001
Pelli Robson contrast sensitivity (log units)				
(range)	0.45 -1.35	0.00 -1.20	0.45 -1.50	Mean difference = 0.49;
(mean ± SD)	1.12 ± 0.22	0.59 ± 0.37	1.13 ± 0.21	p<0.0001

7.1.2.2. Better eye performance versus binocular performance

Binocular performance was plotted against the performance of the better eye for distance acuity, reading acuity and contrast sensitivity. Regression analysis was used to analyse the data (Figure 7.1). For all measurements, data clustered along a straight line and r^2=0.98 for distance acuity; r^2=0.75 for contrast sensitivity and r^2=0.94 for MNREAD acuity. Overall, it was evident that better eye performance was a good predictor of binocular measurements for all clinical tests used. As the slope of the regression line was close to one for all measurements (0.99 for distance acuity; 0.86 for contrast sensitivity and 1.00 for MNREAD acuity), binocular performance changes equally for every unit change in monocular performance. Intercept values of the line were measured near 0 for both distance and MNREAD acuity, while for contrast sensitivity it was 0.16 indicating that binocular and better eye performances were equal for both acuities measurements but binocular performance was slightly better for contrast sensitivity.

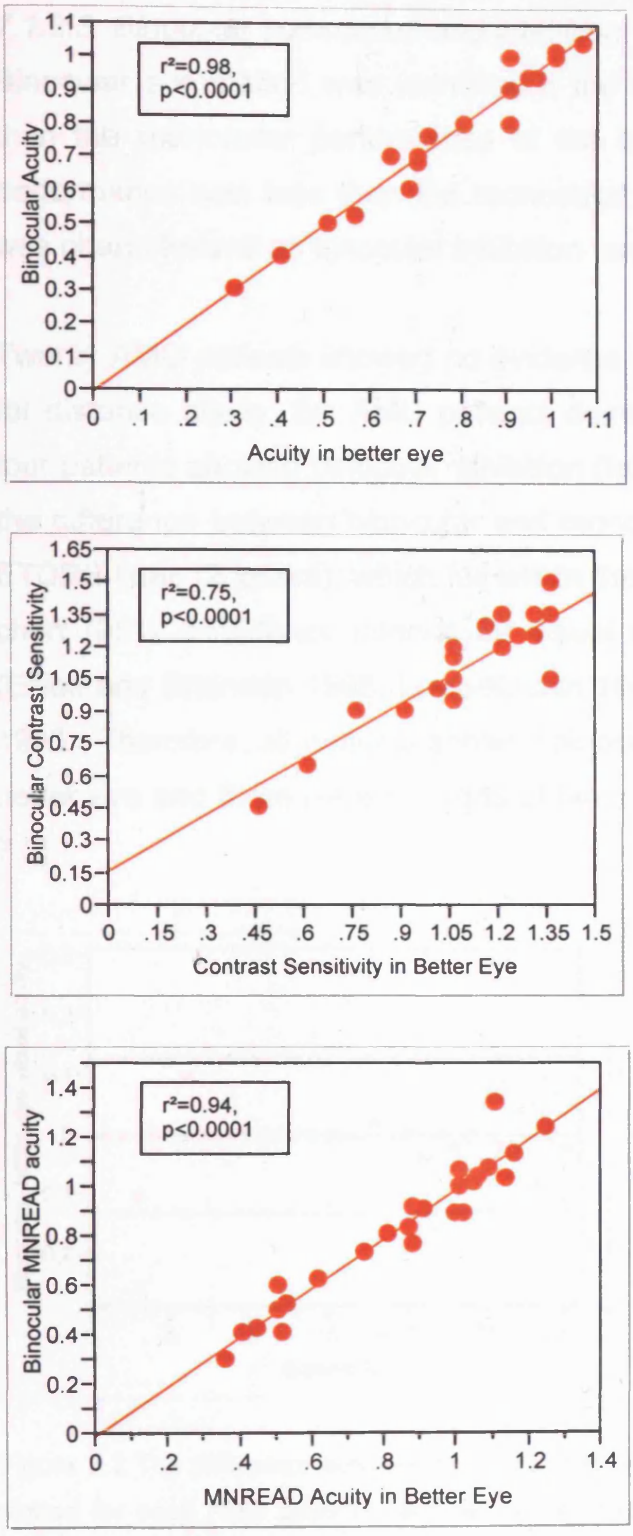


Figure 7.1 *Top figure:* Distance visual acuity of the better eye was plotted against binocular acuity (in log MAR). *Middle figure:* Contrast sensitivity of the better eye was plotted against binocular sensitivity (in log units). *Bottom figure:* MNREAD acuity of the better eye was plotted against binocular MNREAD acuity (in log MAR).

7.1.2.3. Binocular summation and inhibition

Binocular summation was identified if the binocular performance was greater than the monocular performance of the better eye. Wherever the binocular performance was less than the monocular performance of the better eye this was characterised as binocular inhibition (see introduction, section 2.7).

Twenty AMD patients showed no evidence of binocular summation or inhibition for distance acuity. Six AMD patients demonstrated binocular summation and four patients showed binocular inhibition (table 7.2). However, in these patients the difference between binocular and monocular performance averaged 0.004 ETDRS lines (2 letters), which fell within the test retest variability of the ETDRS chart (95% confidence interval for visual acuity scores is: ± 0.13 log MAR) (Elliott and Sheridan 1988; Lovie-Kitchin 1988; Reeves et al. 1991; Rubin et al. 1993). Therefore, all patients showed binocular acuity equal to the acuity of the better eye and there were no signs of binocular inhibition or summation (Figure 7.2).

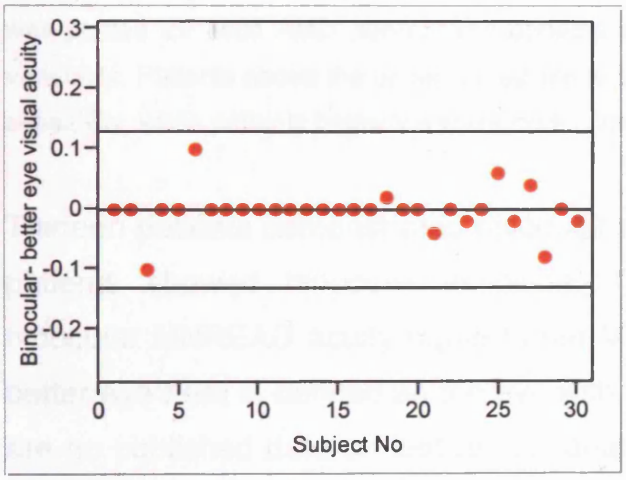


Figure 7.2 The difference between binocular and better eye distance acuity (in log MAR) was plotted for each AMD patient. Each red circle represents one AMD patient. The dotted lines represent the 95% CI of the test –retest variability. Note that all observed differences fell within these limits.

For contrast sensitivity, seventeen patients demonstrated binocular contrast sensitivity equal to the sensitivity of the better eye (for this analysis the better eye was defined as the eye with the better contrast sensitivity), while nine patients demonstrated summation and four patients showed inhibition.

However, the 95% confidence intervals of test-retest variability for contrast sensitivity presented by Rubin et al. (Rubin et al. 1993) was ± 0.12 log units and the average of our patients' performance fell well within these limits (mean 0.02 log units). Thus, only six patients demonstrated summation and two patients showed inhibition as their performances were outside the test-retest variability (Figure 7.3).

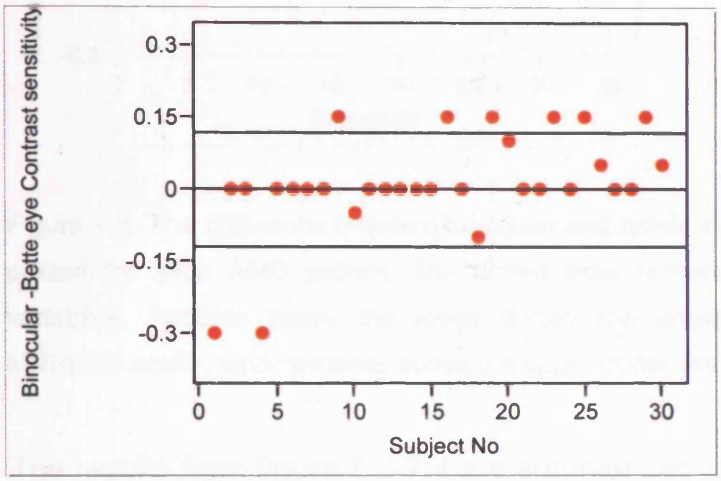


Figure 7.3. The difference between binocular and better eye contrast sensitivity (in log units) was plotted for each AMD patient. The dotted lines represent the 95% CI of the test –retest variability. Patients above the upper dotted line showed binocular summation regarding contrast sensitivity, while patients below the lower dotted line showed binocular inhibition.

Thirteen patients demonstrated binocular summation for reading acuity and five patients showed binocular inhibition. The remaining twelve patients had binocular MNREAD acuity equal to the MNREAD acuity of the better eye (the better eye here is defined as the eye with the better MNREAD acuity). As there are no published data on test-retest variability for the MNREAD chart, analysis of unpublished pilot data from our lab was used to determine the 95% CI for this test (-0.050- 0.065 logMAR). Hence, if this variability was taken into account in this study, five patients showed binocular summation and only two patients showed inhibition (Figure 7.4).

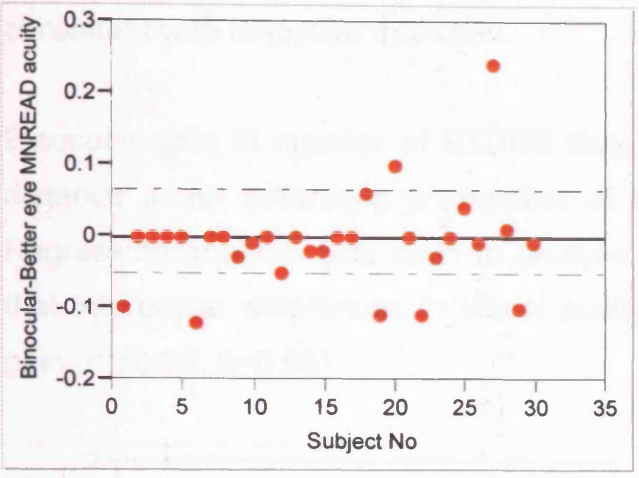


Figure 7.4. The difference between binocular and better eye MNREAD acuity (in log MAR) was plotted for each AMD patient. The dotted lines represent the 95% CI of the test –retest variability. Patients below the lower dotted line showed binocular summation regarding MNREAD acuity, while patients above the upper dotted line showed binocular inhibition.

The results from figure 7.2-7.4 are summarized in Table 7.2.

Table 7.2. % of all AMD cases that demonstrated binocular summation, inhibition or no difference between binocular performance and better eye performance regarding distance and MNREAD acuity and contrast sensitivity. The test-retest variability has been taken into account.

	Binocular Summation	**Binocular Inhibition**	**No difference**
Distance acuity	0%	0%	100%
MNREAD acuity	16.6%	6.6%	76.6%
Contrast sensitivity	20%	6.6%	73.3%

7.1.2.4. Can interocular acuity difference predict binocular performance?

The term 'binocular gain' was used for further analysis of the data in accordance with previous reports (Rubin et al. 2000). We defined binocular gain as the difference between binocular acuity and the acuity in the better eye. Values>0 indicated positive gain which was consistent with binocular

summation, whereas values<0 was indicative of negative binocular gain and consistent with binocular inhibition.

Binocular gain in number of ETDRS lines was plotted against the interocular distance acuity difference (in number of ETDRS lines) for all AMD patients. Regression analysis was used to analyse the data (Figure 7.5) and indicated that interocular differences in visual acuity was a poor predictor of binocular gain (r^2 =0.00, p=0.93).

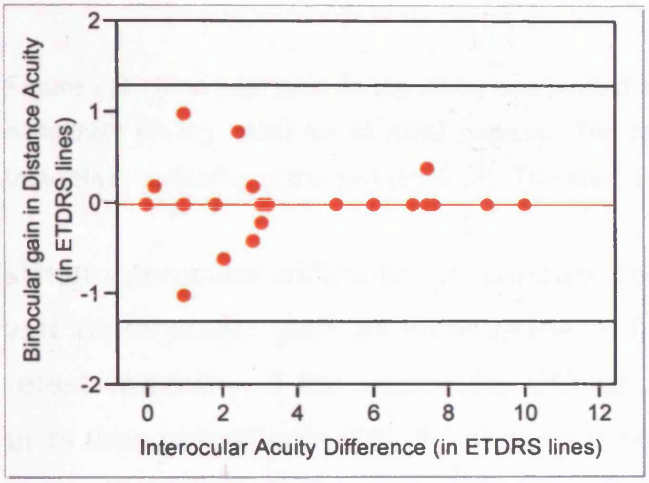


Figure 7.5. Binocular gain in number of ETDRS lines was plotted according to their interocular distance acuity difference (in number of ETDRS lines) for all AMD patients. The area between the dotted lines indicates the test-retest variability of the test (95% CI). The solid line is the best fit linear regression line.

Binocular gain in contrast sensitivity was also plotted against the interocular difference in contrast sensitivity for all AMD patients (figure 7.6). Regression analysis was used to analyse the data and indicated that interocular differences in contrast sensitivity was also a poor predictor of binocular gain (r^2 =0.05, p=0.20).

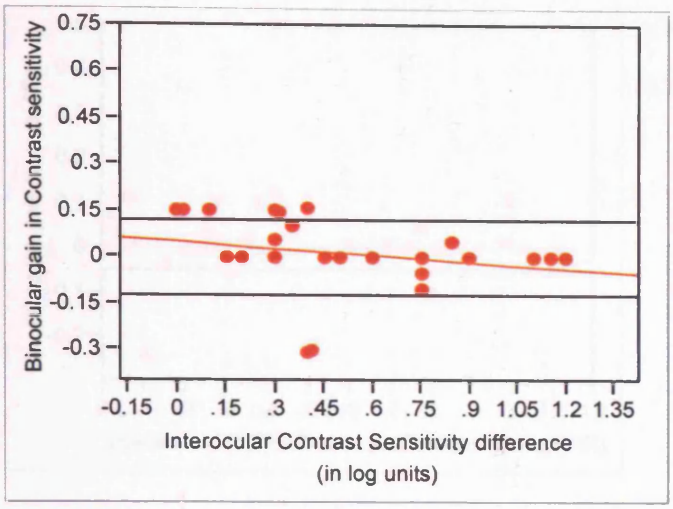


Figure 7.6. Binocular gain (in log units) was plotted against the interocular difference in contrast sensitivity (in log units) for all AMD patients. The area between the dotted lines indicates the test-retest variability of the test (95% CI). The solid line is the best-fit linear regression line.

When interocular difference in contrast sensitivity was more than 0.40 there was no binocular gain, as measurements from all patients fell within the test – retest variability. If the interocular difference was equal or less than 0.40 log units then six patients (46.1%) showed a positive binocular gain (mean positive gain= 0.15 log units) and two patients (15.38%) demonstrated negative binocular gain (mean negative gain=0.3 log units).

Binocular gain was plotted against the interocular MNREAD acuity difference for all AMD patients (figure 7.7). Regression analysis was used to analyse the data (Figure 7.7) and indicated that interocular differences in MNREAD acuity was a poor predictor of binocular gain (r^2 =0.00, p=0.69). There was no obvious trend in figure 7.7 to indicate any change in binocular gain with increasing interocular difference. However, five patients showed a positive binocular gain (mean positive gain was 0.10 logMAR and two patients showed a negative binocular gain (mean negative gain was 0.17 log MAR), if the test-retest variability was taken into account.

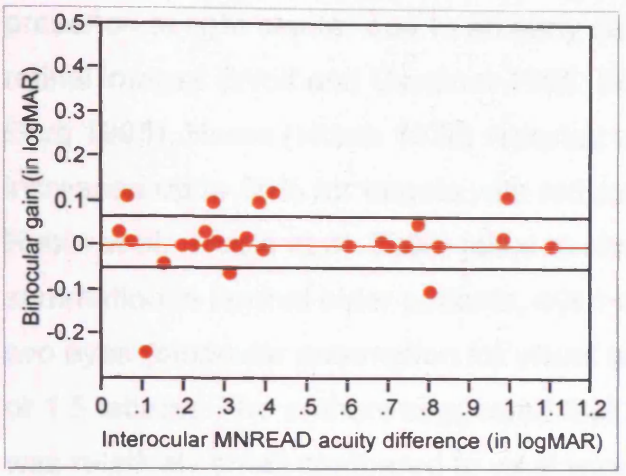


Figure 7.7. Binocular gain in log MAR units was plotted according to the interocular MNREAD acuity difference (in log MAR units) for all AMD patients. The area between the dotted lines indicates the test-retest variability of the test (95% CI). The solid line is the best-fit linear regression line.

7.1.3 Discussion

On average, AMD patients included in this study showed binocular performance equal to the performance of the better eye alone. Our data demonstrated that binocular distance acuities could be inferred from measures of monocular acuity, which was in accordance with the results from Rubin et al. (Rubin et al. 2000). Similar results were obtained for contrast sensitivity and MNREAD acuity.

Distance acuity measurements seemed to have no benefit from binocular viewing as none of the patients showed any binocular gain beyond the test-retest variability. Furthermore, interocular differences in acuities did not play any role with respect to binocular gain in distance visual acuity.

Previous reports on normal young subjects showed an advantage of 10-12% for binocular versus monocular viewing when visual acuities were equal in the two eyes under high luminance and high contrast conditions (Campbell and Green 1965; Home 1978; Cagenello et al. 1993; Horowitz 1994). It has been hypothesized, that older subjects could demonstrate greater binocular summation compared to younger patients due to the following factors. Firstly in older patients, there is a reduction in retinal illumination due to both pupillary miosis and nuclear cataract occurring with age (Weale 1961) and secondly, the

presence of light scatter due to an early cataract, reduces the contrast of the retinal images (Wolf and Gardiner 1965; Bettelheim and Chylack 1985; van den Berg 1995). Home (Home 1978) reported that binocular summation can be increased up to 50% for targets with reduced luminance or contrast. However, Rubin et al. (Rubin et al. 2000) failed to show an increase in binocular summation in normal older patients, even in patients with equal acuities in the two eyes (binocular summation for visual acuity on average was 0.03 logMAR or 1.5 letters). The authors suggested that the loss in illumination or contrast was relatively small compared to what was required to produce increased binocular summation. They also reported little evidence for binocular inhibition when the monocular acuities in the two eyes were unequal in AMD cases, which is in agreement with our data. In support of the latter results, Pardhan (Pardhan 1996; Pardhan 1997) showed reduced binocular summation in both the central and the peripheral visual field for older subjects versus younger ones. She demonstrated that binocular summation was dependent on the monocular difference in sensitivity and the older subjects showed a greater difference between the two eyes at higher spatial frequencies.

According to our results, the majority of AMD subjects demonstrated no improvement in their performance when viewing binocularly versus monocularly with the better eye with respect to contrast sensitivity. We found a benefit in binocular viewing for only a limited number of cases (20%) for contrast sensitivity while 6.65% of AMD patients showed binocular inhibition. More specifically, when the interocular difference in sensitivity was greater than 0.40 log units there was no binocular gain. If the difference was equal or less than this the majority of patients (46.1%) showed a small positive gain (mean positive gain was 0.15 log units) and 15.38% of patients showed negative gain (mean negative gain was 0.3 log units). However, in both cases the binocular gain was relatively small.

Binocular performance for contrast sensitivity measurements in normal subjects is shown to be increased by 42% compared to monocular performance across all spatial frequencies (Blake and Fox 1973; Blake et al. 1981), while unequal monocular contrast sensitivities such as in cataract or in amblyopia reduce binocular summation (Pardhan and Gilchrist 1991; Pardhan and Gilchrist 1992).

Therefore, evidence of binocular inhibition was expected in AMD patients, in cases where unequal sensitivities has been presumed, as in patients with asymmetrical disease. Indeed, the lack of binocular summation and the presence of inhibition regarding contrast sensitivity in AMD patients have previously been reported (Fosse et al. 2001). We recorded binocular inhibition regarding contrast sensitivity in a lower percentage (6.6%) compared with previous reports. More specifically, Valberg and Fosse (Valberg and Fosse 2002) showed that in subjects with normal vision, binocular contrast sensitivity was higher than monocular measurements. In his AMD group, patients demonstrated reduced binocular summation and 8 subjects out of 13 (61%) showed binocular inhibition. In another paper Faubert and Overbury (Faubert and Overbury 2000) also reported a high percentage (almost 50%) of AMD showing binocular inhibition regarding contrast sensitivity. This "inhibition" was not related to the contrast sensitivity of the better eye or to the visual acuities and it was more obvious primarily in images with medium to low spatial frequency components.

Two main factors were suggested by Valberg to explain binocular inhibition in AMD patients (Valberg and Fosse 2002). Firstly, as it was mentioned previously (see introduction, section 1.2), AMD can occur at different times in the two eyes and is often presented with asymmetrical macular scotomas. In these cases, even if binocular retinal correspondence is preserved unequal retinal sensitivities could impair binocular summation. Recent studies (Curcio et al. 2000; Owsley et al. 2000) indicated that rods are more vulnerable to early damage than cones in AMD and asymmetrical disease could cause uneven involvement of the rods between the two eyes. This can possibly lead to same effect as unequal light adaptation of the two eyes according to Valdberg (Valberg and Fosse 2002). Furthermore, additional eye disease such as unilateral cataract or monocular pseudophakia can co-exist with AMD and thus produce dissimilar retinal illumination of the two eyes.

Only 16.6% of AMD patients showed binocular summation in their MNREAD acuity. Furthermore, 6.6% of patients showed binocular inhibition. Interocular differences played no role in binocular gain. Nevertheless, despite the binocular outcome, the overall binocular gain, positive or negative was relatively very

small for MNREAD acuity (mean positive gain 0.10 logMAR and mean negative gain 0.17 logMAR).

In general, our results indicated that binocular viewing versus viewing with the better eye alone may be beneficial for some of the patients with similar sensitivities between the two eyes, especially during some everyday tasks such as seeing steps, curbs, irregularities in the pavement etc. that depend on contrast detection (Dickinson 1998). Furthermore, reading acuity seemed to benefit from binocular viewing in a small number of patients although the interocular differences in acuity did not seem to play a role.

7.2 ASSESSMENT OF BINOCULAR FUNCTION

7.2.1 Methods

Assessment of binocular function of thirty AMD patients was performed using the cover test, the Bagolini striated glasses, a test using a dichoptic fixation target by means of CrystalEyes system and a stereoacuity test (Frisby test). The methodology used was described in detail in the general methods and instrumentation chapter (section 5.3.1 - 5.3.4).

7.2.2 Results

7.2.2.1. Cover test

Five patients (16.6%) showed no movement in either eye to take up fixation when the fellow eye was occluded during the cover test. Five more patients (16.6%) demonstrated a movement in both eyes, while the remaining twenty patients (66.8%) demonstrated a movement only in one eye. In all the latter cases, the eye movement was observed in the worse eye.

7.2.2.2. Bagolini striated glasses

All patients perceived a cross binocularly with four patients (13.3%) reporting the presence of a gap centrally on the cross (see section 5.3.2). We therefore concluded that binocular fusion was retained in all examined AMD patients despite the presence of macular scotomas.

7.2.2.3. Test for binocular fusion

Part one: Identification of a cross

With this test we evaluated patients' ability to fuse the target in a more restricted area near their PRL (5.3.3). According to the results of this test only 10 subjects (33.3%) managed to see a cross. The remaining 20 patients reported seeing only one line with the better eye.

Part two: Identification of letters

The ability to fuse targets in the area adjacent to PRL was preserved in 13 patients (43.3%), as they managed to read all the letters (5.3.3). However, 11 patients (36.6%) read only the letters presented to the better eye. The remaining 6 subjects (20%) read all the letters from the better eye and only one of the two letters from the worse eye.

7.2.2.4. Frisby test

None of the AMD subjects was able to perform the test (5.3.4). Therefore, no stereoacuity measurements were obtained even with the 6mm thickness plate at 30cm (disparity of 600 seconds of arc).

7.2.3 Discussion

The results of the cover test indicated that most of the patients were using different areas to fixate when viewing binocularly versus monocularly (83.3% of patients demonstrated a movement either in both eyes or in the worse eye only).

Binocular fusion was preserved in all studied patients according to the results of the Bagolini glasses test. However, binocular fusion at the fixation locus was preserved only in some AMD cases (33.3%). There is very limited reported data on binocular fusion in AMD patients. Nevertheless, our data were consistent with previously presented results by Schuchard, who reported that only 20% of their AMD patients perceived the visual stimuli binocularly when using a similar test (Schuchard et al. 1995). We also found that binocular function at the area adjacent to PRL was impaired in almost half of the cases (43.3%).

We failed to demonstrate any level of stereocuity in any of the AMD patients.

Studies of stereoacuity measurements in normally sighted people with naturally occurring visual acuity differences between the two eyes showed a significant correlation between stereoacuity and visual acuity differences (r=0.76) (Lam et al. 1996). Furthermore, if the interocular difference in acuity was one line or more the decline was sharper (r=0.88). Neither the acuity in the better nor in the worse eye was related to the reduction in stereoacuity. Stereoacuity measurement studies of normally sighted people with simulated poor acuity (using plus lenses) showed that good stereovision can be obtained with acuity as poor as 6/18 in both eyes (Donzis et al. 1983). However, this type of simulation probably can be best applied to eye conditions such as cataract and not in cases with retinal scotomas. The above authors also produced a nomogram relating Snellen acuities to stereoacuity as measured by the Randot stereoacuity test. Larson and Bolduc (Larson and Bolduc 1991) also induced artificial blur in their study but the effect on stereoacuity varied across subjects. Decreased near acuity in one eye also produced a linear decline in stereoacuity according to Levy and Glick (Levy and Glick 1974). It has also been suggested that equal vision in the two eyes was more important than the absolute level of vision in either eye and three lines of acuity difference between the two eyes would disrupt stereoacuity (Rubin et al. 1997).

As stereopsis arises from horizontal retinal disparities between the two foveas or other corresponding points, the slight lateral displacement of the eyes gives rise to fusion and perception of stereopsis. However, if the displacement is too large, diplopia occurs (Hirsch and Weymouth 1948). When both eyes receive an equally blurred image the two images are fused but the resultant stereoscopic image is too blurred and probably inadequate to provide sufficient information regarding depth. Therefore, stereopsis cannot be predicted by monocular thresholds alone (McKee et al. 1990) as both monocular sensitivities can limit stereoacuity individually. Moreover, stereoacuity seems to be affected more by the presence of a blurred image in one eye only (Westheimer and McKee 1980).

Only limited studies of stereoacuity in patients with retinal and optic nerve disorders exist. Patients with optic nerve disease showed a disproportionately

greater reduction in their stereoacuity compared to what was expected from the normal nomograms (Friedman et al. 1985). According to Shah et al. (Shah et al. 1995) patients with retinal disease did not differ significantly from patients with optic nerve disease in terms of stereocuity loss as predicted from the published nomogram. They concluded that patients with Snellen acuity no better than 20/30 in even one eye are likely to have abnormal stereoacuity. Their results were verified by using different stereoacuity tests (such as the Titmus, the Randot and the TNO stereoacuity test) and they reported that an abnormal score in one test was predictive of the abnormality in the rest of the tests. Although we used the Frisby test to assess stereoacuity in our patients previous reports comparing different clinical stereotests (Titmus, TNO, Frisby and two-needle tests) showed low but significant correlation between them (Hall 1982).

Although none of our subjects had distance visual acuity better than 0.3 log MAR (equivalent to 6/15 Snellen acuity) in both eyes and at the same time less than three lines of acuity difference between the two eyes, we decided to test stereocuity in our subjects as some studies were only based on simulating eye diseases and only limited data existed for AMD patients. Nevertheless, our results failed to demonstrate any level of stereocuity in any of our patients. Valberg and Fosse (Valberg and Fosse 2002) proposed that the presence of asymmetrical macular scotomas leading to unequal retinal stimulation is the reason for the reduced binocular acuity, contrast sensitivity and even impaired stereopsis that AMD patients are experiencing.

7.3. SUMMARY

Overall, binocular performance was equal to the performance of the better eye alone. Therefore, estimation of patients' performance could be based on monocular measurements and separate assessment of binocular data is not required.

There was no binocular gain with respect to distance visual acuity. Regarding contrast sensitivity and MNREAD acuity a binocular gain was observed although it was relatively small (either positive or negative gain). For contrast sensitivity the binocular gain was observed only when the interocular difference

in sensitivity was equal to or greater than 0.4 log units. There was no similar trend for MNREAD acuity.

In general, the cover test suggested that most of the AMD patients included in this study used a different retinal locus to fixate under binocular compared with monocular viewing. Binocular fusion was preserved in all AMD patients' according to the results of the Bagolini glasses test. However, binocular fusion at the fixation locus and at the area adjacent to PRL was preserved only in some AMD cases (33.3% and 43.3% respectively). None of the patients demonstrated any level of stereocuity.

CHAPTER 8

MONOCULAR VIEWING CONDITIONS: PRLs AND MAPPING OF MACULAR SCOTOMAS

The concept of the preferred retinal locus in AMD patients has already been discussed in the introduction (section 1.3). Although many techniques have been employed in the past to locate PRLs on the retina and their position with respect to the scotomas, the instruments most used in recent years are the Scanning Laser Ophthalmoscopes (Timberlake et al. 1986; Timberlake et al. 1987; Culham et al. 1992; Schuchard and Raasch 1992; Guez et al. 1993). In this chapter by means of an SLO the macular scotomas will be identified and their effect on the position of the monocular PRLs used by the subject during a fixation task will be assessed.

Chapter 8 is divided into seven sections. Initially, the monocular retinal locus used for fixation will be identified in each eye for all AMD patients (8.1.1) and the macular scotomas will be accurately measured using the scanning laser ophthalmoscope (8.1.2 and 8.1.3). Next, the distance of monocular PRLs from the previously normal fovea will be calculated (8.1.4). The effect of the interocular symmetry or asymmetry of macular scotomas on retinal eccentricity and correspondence of the monocular PRLs will be also assessed (8.1.5 - 8.1.6). Finally, whether SLO data (scotoma size and retinal eccentricity of PRLs) are good predictors of distance and MNREAD acuity and contrast sensitivity will be investigated in the last two sections (8.1.7).

In this chapter hypothesis 1 will be explored (4.3).
According to hypothesis 1:
AMD patients with symmetrical central scotomas are more likely to have preferred retinal loci with similar retinal eccentricities in both eyes under monocular viewing conditions than patients with asymmetrical scotomas. Therefore, their PRL in the two eyes are more likely to fall on more corresponding retinal areas than in patients with asymmetrical scotomas.

Furthermore in this chapter we will address the question whether SLO data (scotoma size and retinal eccentricity of PRL) are good predictors of clinical performance (distance and MNREAD acuity and contrast sensitivity).

8.1. Methods

To determine the retinal location used for monocular fixation, as well as to determine macular scotomas, a confocal scanning laser ophthalmoscope was used (Chapter 5.4.1). As previously described, the Rodenstock SLO includes a helium-neon laser as the primary source for the fixation target as well as for the visual stimuli, which are presented in positive contrast, while the fundus is visualized using the infrared laser.

Thirty patients with bilateral AMD were included in the study. The test was performed for both eyes. Each subject was seated against the SLO without his spectacles and his distance correction was added to the SLO computer. The field size used was 40° and the image resolution was 786 by 576 pixels. The background luminance of the SLO screen was set at 125cd/m^2 (Chapter 5.6.2).

8.1.1. Monocular retinal locus used for fixation

Recordings were performed monocularly with each eye, while the fellow eye was occluded. The fixation target was a disk with a total diameter of 2.2° and a central opening of 0.4° diameter. The target was first displayed in the centre of the SLO screen and the subject was instructed to move his eye so that the central opening of the fixation target was best seen. When the patient verified that this had been achieved, the fixation was registered by the system. The same procedure was repeated for the fellow eye. Ideally, the blind spot, the scotomas, and the fixation locus should be included in the captured image. However, if the patient was using an exceptionally peripheral retinal area to fixate that was not always feasible. In that case the fixation target was moved to a more peripheral location on the SLO screen so when patient was fixating the target at its new location a more satisfactory retinal image could be obtained.

8.1.2. Mapping of retinal scotomas

The size of macular scotomas was measured using SLO microperimetry (5.4.1). The fixation target used was the same disk as the one described above (8.1.1),

which was displayed in a similar fashion. The patient was given the same instructions in order to fixate the target and he was asked to keep his fixation as steady as possible during the entire test. The size of the testing stimulus used was Goldmann III and it was presented for 200ms. As SLO microperimetry can be a prolonged and tiring test, especially with low vision patients, we only used one stimulus intensity, 0db (equivalent to luminance ~200cd/m^2). Therefore, the borders for deep scotomas only were identified. We defined these scotomas as 'absolute' scotomas.

Initially, the examiner had to position the visual stimuli manually at different retinal locations. Moreover, between stimuli presentations the examiner also had to select a retinal feature such as a retinal lesion or a vessel bifurcation, in order to compensate for eye movements and therefore, accurately test points on the fundus image. As in that way the test was time consuming for both the examiner and the patient, software was developed in order to track and correct automatically for eye movements during the test (in cooperation with Dr C Bellmann). A grid pattern of testing stimuli was randomly presented. In particular, a circular grid with four radii and four regularly spaced points per radius was superimposed over the scotomatous area. Manually projected stimulus could be added at the end of the testing grid. During the stimulus presentation the patient was asked to respond to the appearance of each stimulus by pressing a button and a microperimetry map was constructed at the end of the session superimposed on the fundus image. A video recorder was also used to save the retinal movements during the microperimetry session.

8.1.3. Measuring scotoma size

Scotomatous areas were measured using SLO images and microperimetry results. The scotoma area was manually encircled with a line directed by moving the computer's mouse using a programme written with the Matrox Imaging Library and the area was calculated automatically. Similar methods have been employed by other investigators in the past in order to measure the size of retinal lesions based on SLO images (Bellmann et al. 2002; Bellmann et al. 2003) or colour photos (Sunness et al. 1999). For this project the scotomatous area was measured by the programme in pixels^2 and was

converted to min of arc². The area of the optic disc was also measured manually in ten subjects using the same programme and the average value (mean disc area = 22.5 degrees ²) was used to define the disc area used in our calculations. Scotoma sizes were subsequently described in optic disc areas (DA). Although it has been shown that optic disc size depends on the refractive error of the eye, for refraction between -8.00 DS and +4.00 DS the differences were not significant and therefore, mostly independent (Jonas 2005). As the refraction for all patients fell within this area we used the same average disc area to measure their retinal scotomas.

8.1.4. Distance of monocular fixation from 'fovea'

The distance between monocular fixation and the fovea was calculated for both eyes for all tested subjects. As the fovea was affected by AMD its location could not be accurately seen on SLO images and we used an indirect way to measure these distances. Initially, the centre of the blind spot was located on the SLO images of the patients' fundus using a method that has already been described in this study (section 6.2). Subsequently, we used the mean values of the horizontal and vertical eccentricity of the normal fovea to the centre of the blind spot found during SLO testing for the older group (16.4° and 2° respectively) (section 6.1.4) in order to estimate the foveal location. Afterwards, the distance between the fovea and the monocular fixation locus was calculated for each eye (in degrees of visual angle) based on the SLO images. We referred to this distance as DMFF (distance from monocular fixation to fovea) and it was defined as the vector sum of the horizontal and vertical difference between the fovea and the PRL.

The location of fixation locus relative to the scotoma was also assessed. We used the most dominant direction to describe this relationship (Sunness et al. 1996).

8.1.5. Interocular symmetry/ asymmetry of macular scotomas and its effect on retinal eccentricities of the PRLs of both eyes.

Macular scotomas were defined as symmetrical if the interocular difference in their size (in disc areas) was equal or less than one disc area. If their difference

was larger than one disc area they are defined as asymmetrical scotomas. Regression analysis was used to assess if interocular difference in scotoma size was a good predictor of the interocular difference in retinal eccentricities of the monocular PRLs.

8.1.6. Assessment of retinal correspondence of monocular PRLs

In order to evaluate the retinal correspondence between the monocular PRLs in the two eyes we initially calculated the distance between the two fixation loci.

Polar coordinates were used to describe the distance between the monocular fixation loci used by the two eyes by calculating the magnitude of the distance (the vector sum of the horizontal and vertical difference between the two loci) and the angle between them. Subsequently, these distances were calculated separately in the horizontal meridian and in the vertical meridian in order to assess retinal correspondence of the monocular PRLs for patients with symmetrical and asymmetrical scotomas.

8.1.7. Prediction of clinical performance based on SLO data

Regression analyses were also used to determine if scotomas size and/or retinal eccentricity of monocular PRLs were good predictors of distance acuity, contrast sensitivity and MNREAD acuity.

8.2. Results

8.2.1. Monocular fixation and mapping of macular scotomas

Data for monocular fixation and microperimetry results were obtained from thirty AMD patients (fifty eight eyes). Two patients (subjects 5 and 15) failed to perform the test with their worse eye. In those patients the macular lesions were very large, monocular fixation was very unstable and recording of the retinal location of their PRLs and mapping of their scotomas were not possible.

Five patients were tested with the manual microperimetry technique and twenty five patients using the automated grid pattern (Figure 8.1).

Figure 8.1 SLO infrared images of the right fundus of two AMD patients with microperimetry maps of the scotomatous areas. Microperimetry on the first patient (first picture) has been performed manually while on the second patient (second picture) a grid pattern has been used to map the macular scotoma but additional stimuli have also been added manually at the end of the grid. The red cross represents the retinal locus used during fixation of the target. The blue cross indicates the centre of the area that was used as a landmark to compensate for eye movements. Red closed symbols represent 'seen' areas while red open dots represent 'not seen' areas.

Overall, from fifty eight eyes, 17 eyes (29.3%) used a PRL below the scotoma in visual space, 15 eyes (25.8%) used a PRL to the left of the scotomas and 10 (17.2%) to the right, while only 6 eyes (10.3%) showed a PRL above the scotoma in visual space. From the remaining 10 eyes three of them had multiple scotomatous areas (all were the better eye for the patient) and they were fixating with a central normal retinal area, while the rest (7 eyes) were fixating within the scotoma, presumably on an island of a relatively normal function. The latter ones all were the worse eye for the patient apart from two eyes that were the better and worse eye for the same patient. The PRL location with respect to visual field is presented in summary in table 8.1 below.

Table 8.1 PRL location with respect to macular scotomas in visual field space

PRL position in visual space	**Percentage of patients**
Below of the scotoma	29.3%
Left of the scotoma	25.8%
Right of the scotoma	17.2%
Above of the scotoma	10.3%
On an island of vision within the scotoma	12%
On a normal central area among multiple scotomas	5.1%

From the patients who placed their PRL outside the scotomatous area most of them placed it very close to the borders of the scotomas. Only two cases used a PRL further away from the scotomas boundaries (subject 17 in both eyes and subject 21 in the worse eye).

8.2.2. Measuring macular scotomas

In Figure 8.2 an example is presented of how the software was used in order to measure the macular scotomas.

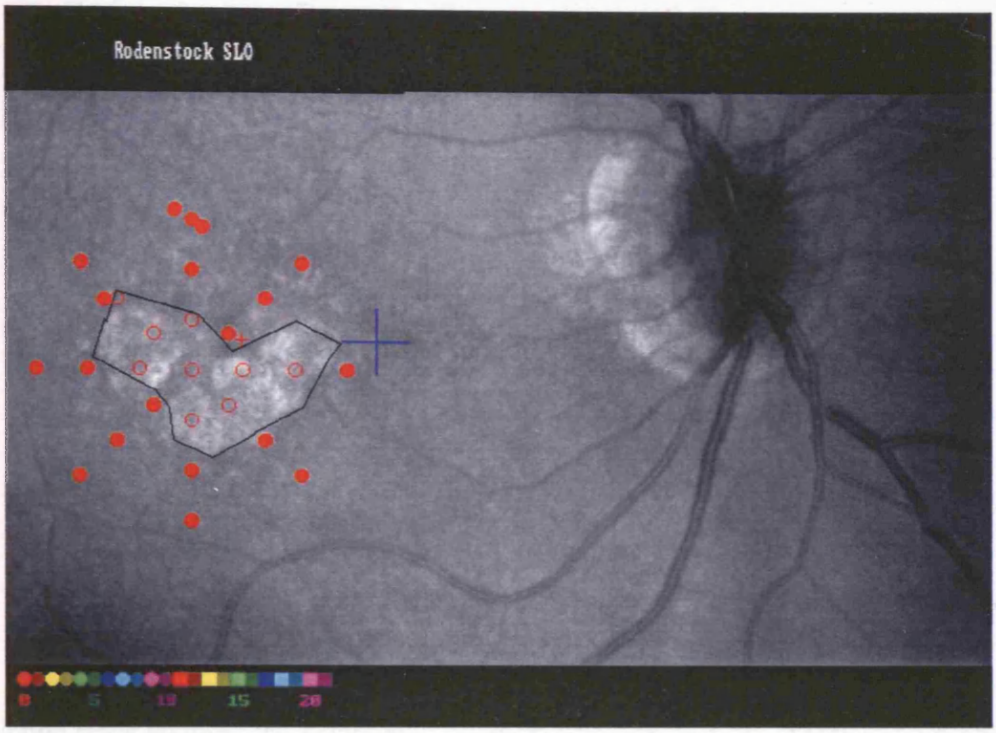


Figure 8.2. Same SLO infrared image with figure 8.1 of the second AMD patient. The area of the scotoma has been manually encircled by a black line based on the borders of the macular lesion on the SLO image and the microperimetry results.

Overall, the mean scotoma size was 4.6 ± 3.6 disc areas (range 0.08 – 13.3). The mean scotoma size in the better eye was 3.1 ± 2.9 disc areas (range 0.08 – 9.5) and the mean scotoma size in the worse eye was 6.2 ± 3.7 disc areas (range 0.5 – 13.3) (Figure 8.3). A detailed table of the scotomas size for all tested patients is presented in appendix 2 (table 8.a). As expected the worse eye had significantly larger scotoma size than the better eye (mean difference=3.1 disc areas; paired t-test, $p<0.0001$).

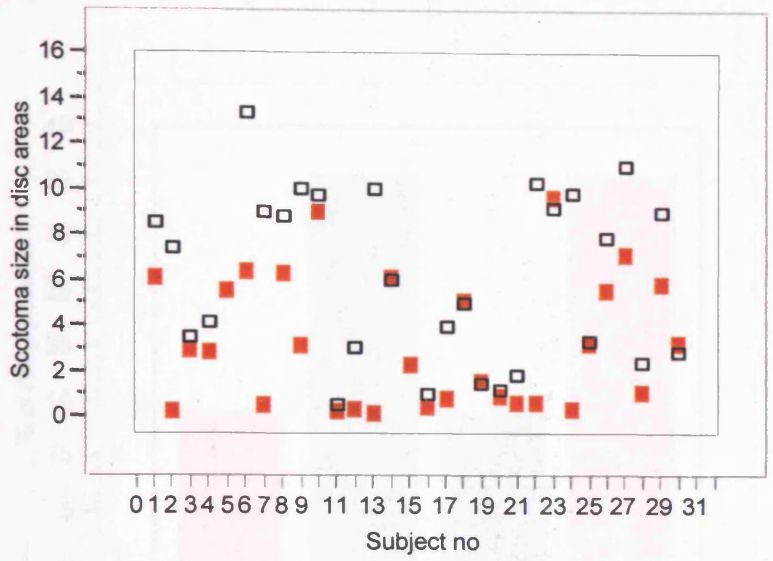


Figure 8.3. Scotoma size in disc areas for both eyes (better and worse eye) are presented for each subject separately. The filled red squares represent the better eye of each subject and the open black squares the worse eye. Subjects no 5 and 15 have only data from their better eye.

Figure 8.4 plotted the scotoma size in the right eye against the scotoma size in the left eye for all AMD patients. There was a weak correlation between the two measurements ($r = 0.21$; $p>0.27$).

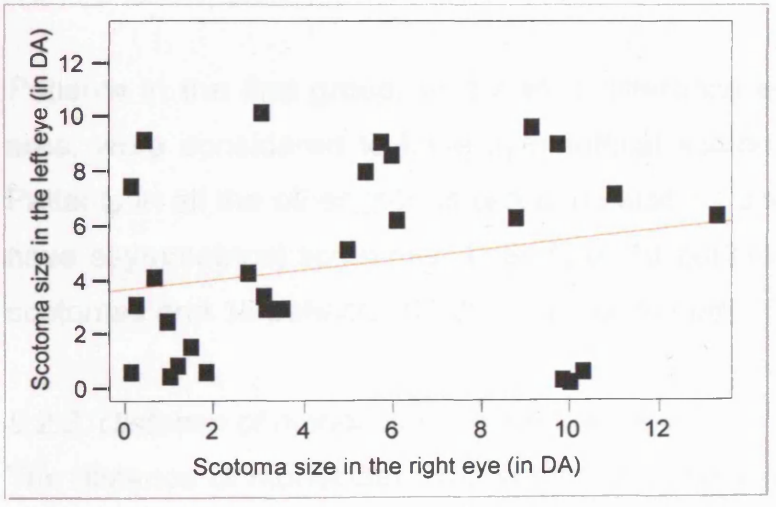


Figure 8.4 Scotoma size in the right eye is plotted against the scotomas size in the left eye. Scotomas sizes have been measured in disc areas (DA).

Consequently, we separated patients with more symmetrical disease from others. Patients were divided in four groups according to the interocular differences in scotoma size: ≤ 1DA, >1- ≤ 2 DA, >2- ≤3 DA and > 3 DA (Figure 8.5).

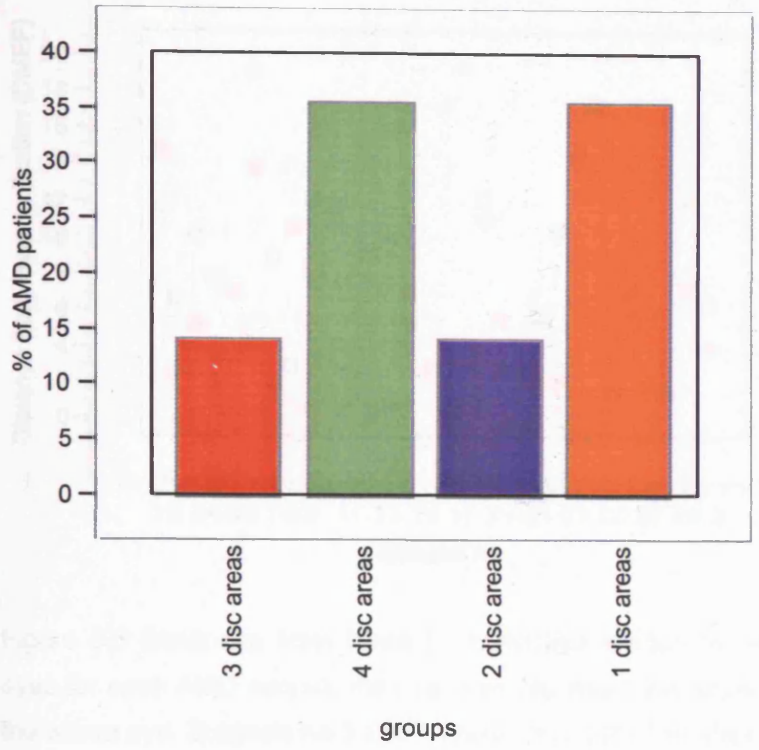


Figure 8.5 Proportion of AMD patients showing interocular differences in scotoma sizes (in DA) is plotted by each group (1DA: ≤ 1DA, 2DA: >1- ≤ 2 DA, 3DA: >2- ≤3 DA and 4DA: > 3DA).

Patients in the first group, who had a difference equal or less than one disc area, were considered to have symmetrical scotomas between the two eyes. Patients in all the other groups (scotoma size >1 disc area) were considered to have asymmetrical scotomas. Therefore, 10 patients (35.7%) had symmetrical scotomas and 18 patients (64.2%) had asymmetrical macular scotomas.

8.2.3. Distance of monocular fixation from 'fovea'

The distance of monocular fixation from the fovea was calculated for each eye separately for the horizontal and vertical axis. The vector sum of the horizontal and vertical difference between the fovea and the PRL was used to define the DMFF (distance from monocular fixation to fovea). A table of the results is presented in appendix 2 (table 8.a). Figure 8.6 presents the DMFF for both eyes for all tested AMD subjects. All data were calculated in pixels and were converted to degrees of visual angle. 1° of visual angle corresponds to ~23 pixels on the SLO monitor screen (Chapter 5.5.1).

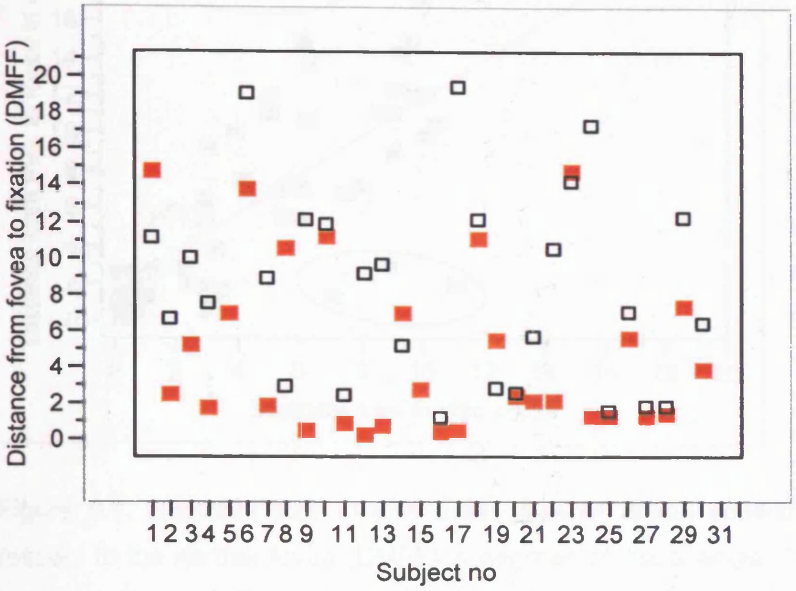


Figure 8.6 Distances from fovea to monocular fixation locus (DMFF) are presented for both eyes for each AMD subject. Red squares represent the better eye and black squares represent the worse eye. Subjects no 5 and 15 have only data from their better eye.

8.2.4. Can scotoma size predict retinal eccentricity of monocular PRL?

Scotoma size is plotted against the retinal eccentricity of the PRLs from the normal fovea (DMFF) for all fifty eight tested eyes in figure 8.7. Regression analysis indicated that scotoma size is a relatively good predictor of the eccentricity of the PRLs' position (r^2= 0.49, $p<0.0001$). The slope of the regression line was 1.01, which shows that the retinal eccentricity of the PRL increases equally for every unit change (disc area) in scotoma size. Intercept value of the line was measured as 1.76 indicating that even for very small scotomas (in disc areas) there is retinal eccentricity of the PRL by at least 1.76°.

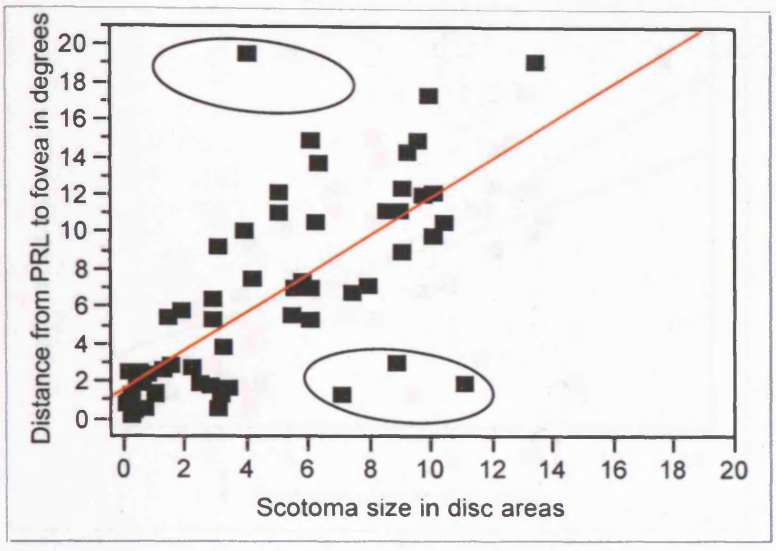


Figure 8.7. Scotoma size in disc areas against retinal eccentricity of monocular PRLs with respect to the normal fovea (DMFF) in degrees of visual angle. The encircled areas contain the outliers in the data. The red line is the best fit linear regression line for the data

As a tighter relationship was expected between scotomas size and retinal eccentricity of the PRLs, the outliers seen in figure 8.7 were evaluated on an individual basis. The point that is encircled in the top circle is the left eye (worse eye) of subject 17 who fixated away from the borders of the scotomas and therefore, his DMFF is larger compared to what it is expected based on the size of the scotomas. The other three points within the lower circle represent eyes that they all fixated on an island of vision within the scotomas and thus DMFF distances were smaller than expected based on the large scotoma sizes (see section 8.2.1).

We also plotted scotoma size and retinal eccentricity of the PRLs separately for the better and the worse eye (figure 8.7a).

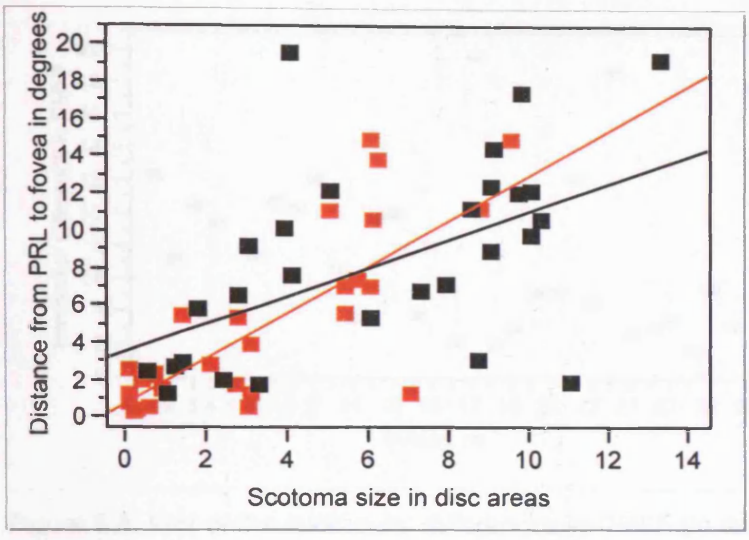


Figure 8.7a. Scotoma size in disc areas against retinal eccentricity of monocular PRLs with respect to the normal fovea (DMFF) in degrees of visual angle for the better and the worse eye. Black symbols represent the better eye and red symbols the worse eye. The black solid line is the best fit linear regression line for the better eye and the red line for the worse eye.

Regression analyses indicated that scotoma size was a better predictor of the eccentricity of the PRLs' position in the better eye compared with the worse eye (r^2= 0.57, $p<0.0001$ for the better eye versus r^2= 0.28, $p=0.004$ for the worse eye). However, there was no significant difference between the two regression lines (ANCOVA, $p=0.18$).

8.2.5. Is symmetry or asymmetry of macular scotomas a good predictor of difference in retinal eccentricity of monocular PRLs between the two eyes?

We also plotted the interocular difference in DMFF for all tested AMD patients (Figure 8.8). The magnitude of these differences ranged from 1.27° to 19.13° of visual angle (median 5.61°).

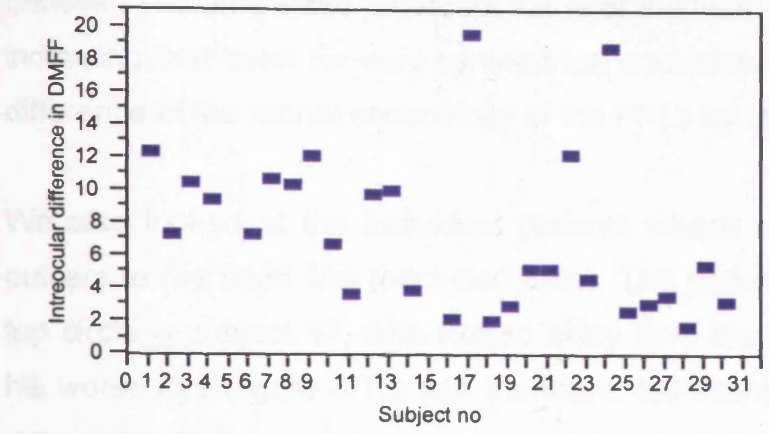


Figure 8.8. Plot of the interocular differences in DMFF (in degrees of visual angle) for all tested AMD patients.

Interocular difference in scotomas size was plotted against the interocular difference in retinal eccentricity (DMFF) for all tested patients (Figure 8.9).

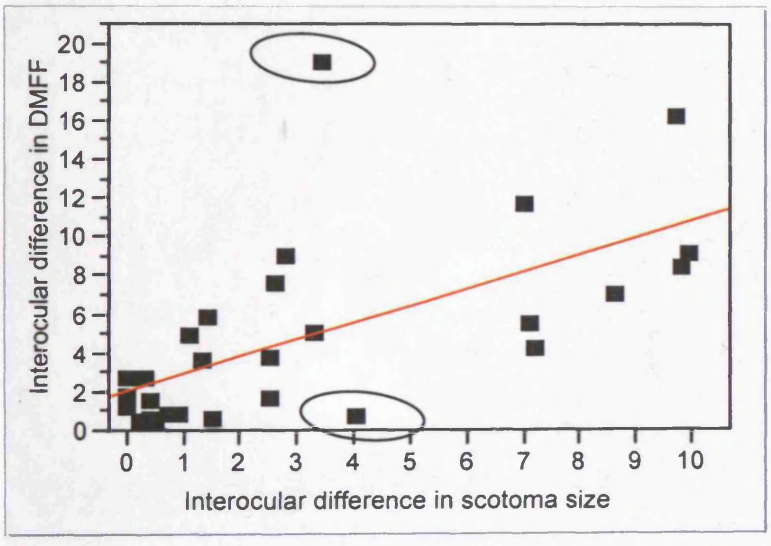


Figure 8.9. Interocular differences in scotomas size (measured in disc areas) against interocular difference in retinal eccentricity of monocular PRLs with respect to the normal fovea (DMFF) in degrees of visual angle. The encircled areas contain the outliers in the data. The red line is the best fit linear regression line for the data.

Regression analysis indicates that interocular difference in scotomas size is a relatively good predictor of the difference in retinal eccentricity of the monocular PRLs used by the patient ($r^2 = 0.37$, $p=0.0007$). The slope of the regression line was 0.88, which shows that the difference in retinal eccentricity of the PRLs increases by 0.88 for every unit change (disc area) in the interocular difference

between scotoma sizes. Intercept value of the fitted line was measured as 2.02 indicating that even for very symmetrical scotomas (in disc areas) there is still difference in the retinal eccentricity of the PRLs by at least 2.02 °.

We also looked at the individual patients whose data produce the two main outliers to the fitted line (encircled data). The patient that is represented in the top circle is subject 17, who fixated away from the borders of the scotomas in his worse eye (figure 8.10) and therefore, his interocular distance between his monocular PRLs is larger compared to what it is expected based on the difference in the scotomas sizes. The patient within the lower circle is subject 27 who fixated on an island of vision within the scotomas in both eyes and thus despite the difference in scotomas size between the eyes his interocular distance from the monocular PRLs to the foveas is relatively small.

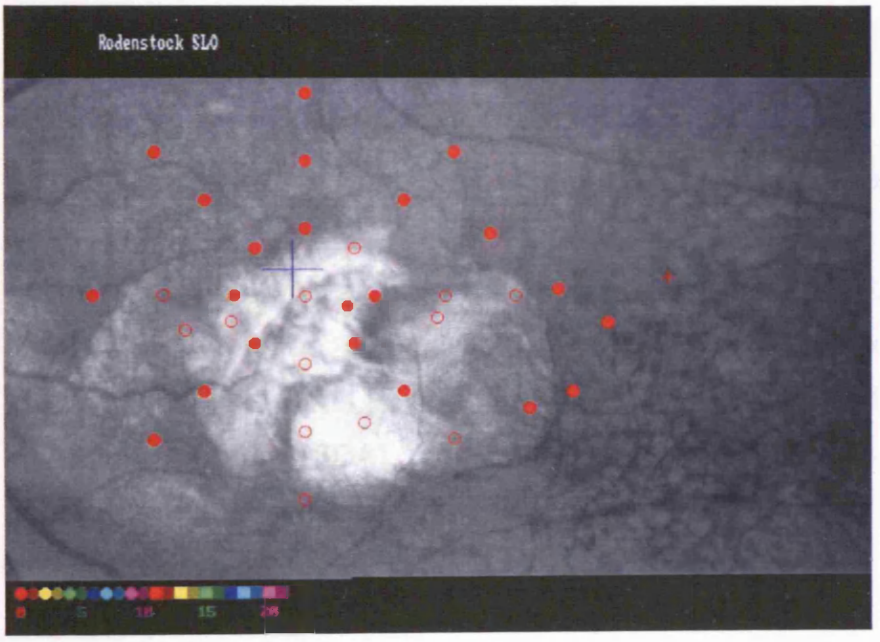


Figure 8.10 Same SLO infrared image of patient no 17. The area of the scotoma has been mapped initially with a grid but additional stimuli have also been added manually at the end of the grid. Note that this patient fixates further away from the borders of the 'absolute' scotomas (red cross).

We also looked into the DMFF differences in the four groups (≤ 1DA, >1- ≤ 2 DA, >2- ≤3 DA and > 3 DA) discussed in 8.2.2 (Figure 8.11). Note that the median value is 1.07°, 3.57°, 5.58° and 7.69 ° accordingly for each group. It is evident that for the first group with symmetrical scotomas (≤ 1DA) the retinal

eccentricities are similar, while for the other groups the retinal eccentricities of the monocular PRLs are different between the two eyes.

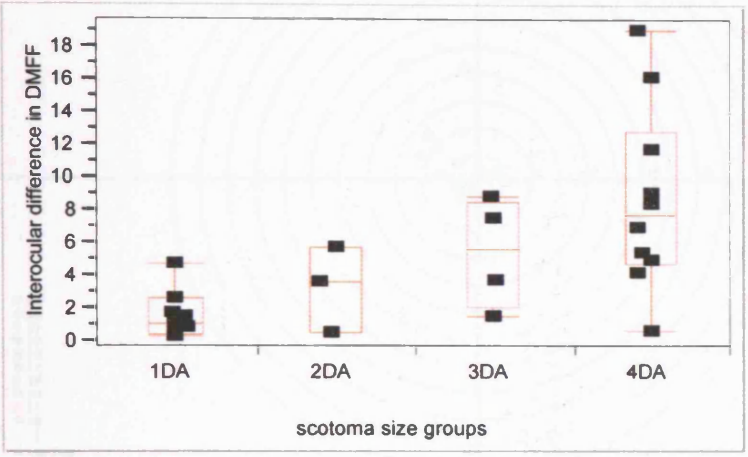
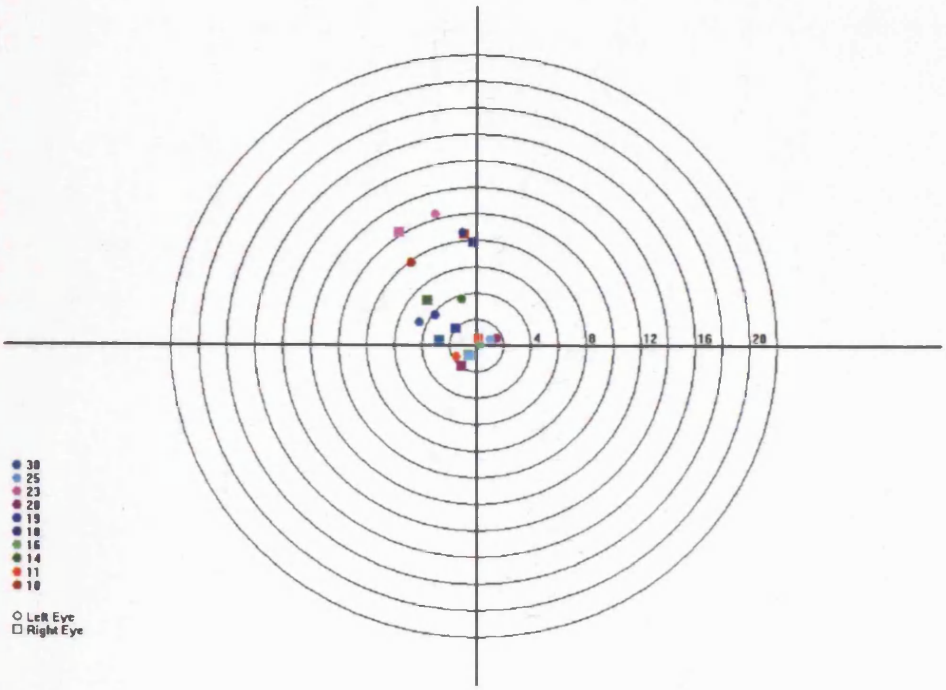


Figure 8.11. The distributions of interocular differences in the distance between PRL locus and fovea (DMFF) are plotted for AMD patients grouped according to their interocular difference in scotoma size (in disc areas). Each distribution is summarized by a quantile box plot showing the 90^{th}, 75^{th}, 50^{th} (median), 25^{th} and 10^{th} percentiles.

8.2.6. Assessment of retinal correspondence of monocular PRLs between the two eyes.

Figure 8.12 maps the actual location of the monocular PRLs on the retina with respect to the fovea separately for patients with symmetrical (≤ 1DA) and asymmetrical scotomas (divided in two further groups for descriptive purposes: >1- ≤ 3 DA and > 3DA). The location of the PRLs has been calculated in degrees of visual angle.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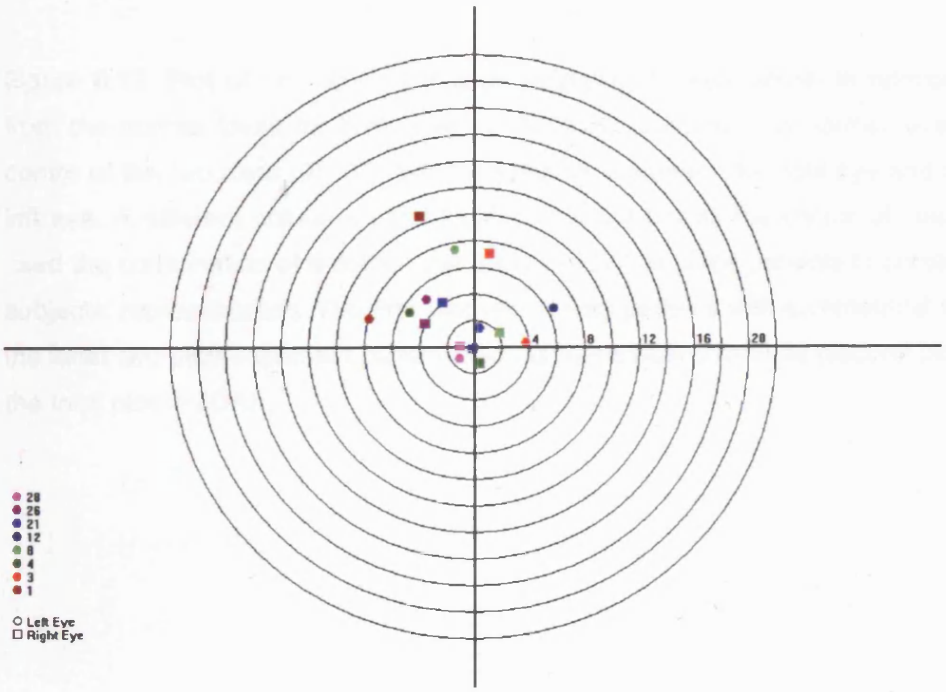
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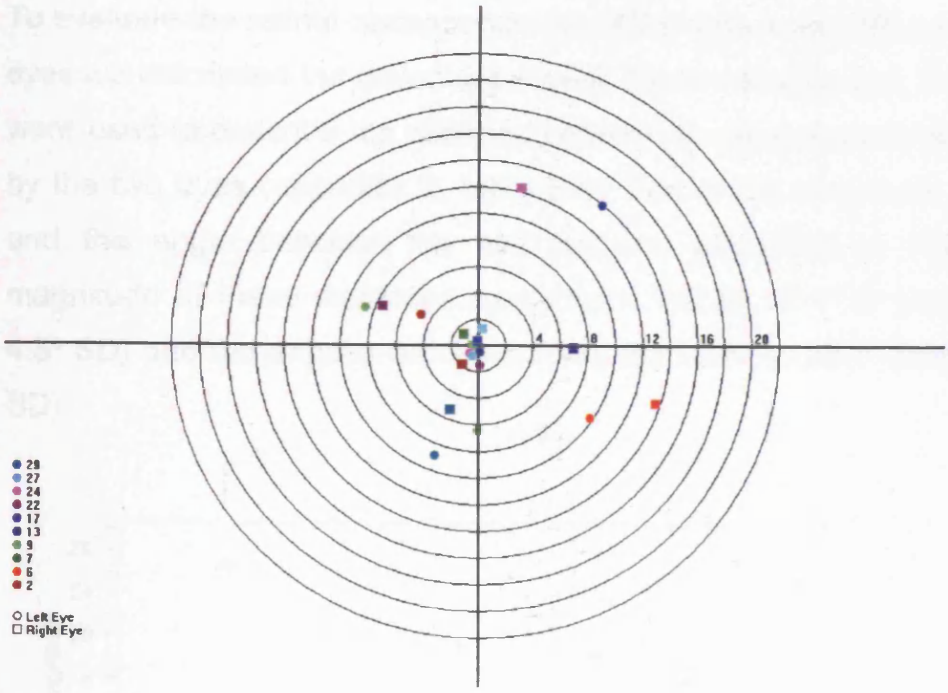


Figure 8.12. Plot of monocular PRLs (in degrees of visual angle) in relation to their distance from the normal fovea for both eyes on 28 AMD patients. The normal fovea is placed in the centre of the two axes (0°, 0°). Square symbols represent the right eye and round symbols the left eye. A different colour is used for each patient but as the choice of colour was limited we used the combination of a colour and a symbol (+) for some patients to create more choices for subjects' representation. The first plot represents patients with symmetrical scotomas (≤ 1DA), the latter two plots represent patients with asymmetrical scotomas (second plot: >1- ≤ 3 DA, and the third plot :> 3DA).

To evaluate the retinal correspondence of the monocular PRLs between the two eyes we calculated the distance between the two fixation loci. Polar coordinates were used to describe the distance between these monocular fixation loci used by the two eyes (appendix 2, table 8.a). Plot of the magnitude of the distance and the angle between the two loci are presented in Figure 8.13. The magnitude of these distances range from 1.2° to 19.1° of visual angle 6.9° ± 4.8° SD) and the angular difference vary from 2.6° to 88.1° (mean 44.0°± 24.3° SD).

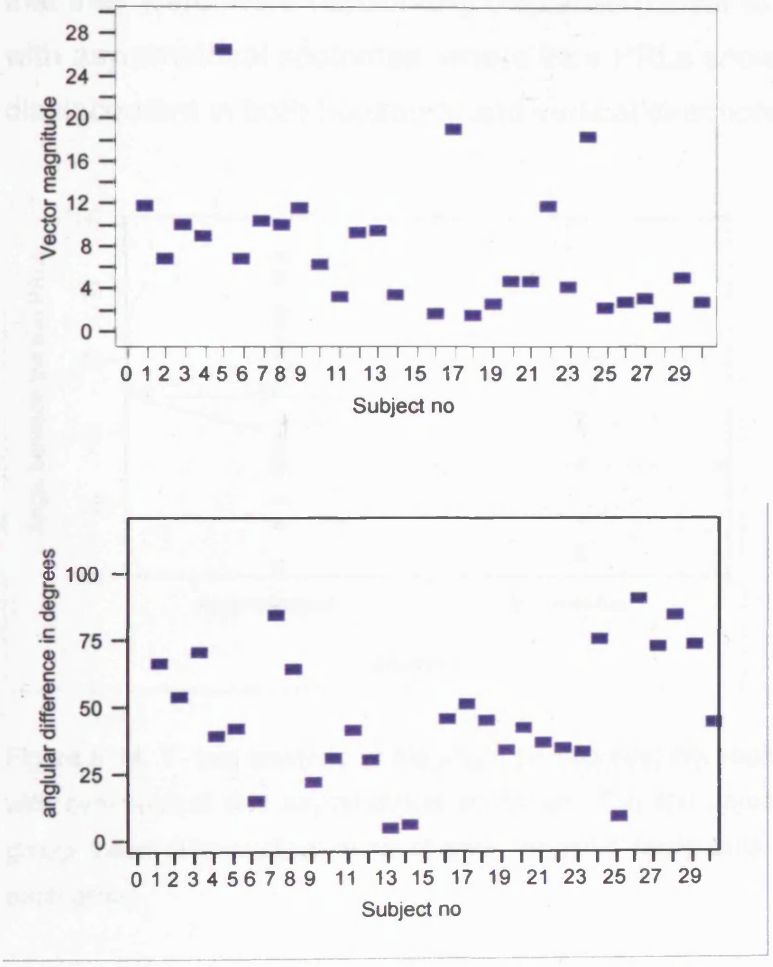


Figure 8.13. The magnitude (top figure) and the angular difference (bottom figure) of the intraocular difference between monocular PRLs for all tested subjects were plotted.

The distance between the monocular PRLs position and the angle between them were measured separately for AMD patients with symmetrical (intraocular difference in scotoma size ≤1 disc area) and asymmetrical scotomas symmetrical (intraocular difference in scotoma size >1 disc area). In patients with symmetrical scotomas the mean distance between the two loci was 3.2° ±

1.4° SD, while in patients with asymmetrical scotomas the mean distance was 8.9° ± 4.8° SD. There was significant statistical difference between the two groups (unpaired t-test; p-value=0.0012) with smaller distances recorded in patients with symmetrical scotomas. With respect to the angle between the monocular PRLs between the two eyes patients with symmetrical scotomas demonstrated a mean of 30.9° ± 14.5° SD and patients with asymmetrical scotomas had a mean of 51.6° ± 25.7° SD. Unpaired t-test between the latter two groups showed statistical significant results (p-value=0.04) (Figure 8.14), which indicated that patients with symmetrical scotomas demonstrated PRLs that they were more horizontally displaced (closer to 0°) compared with patients with asymmetrical scotomas, where their PRLs showed greater diversity in their displacement in both horizontal and vertical directions.

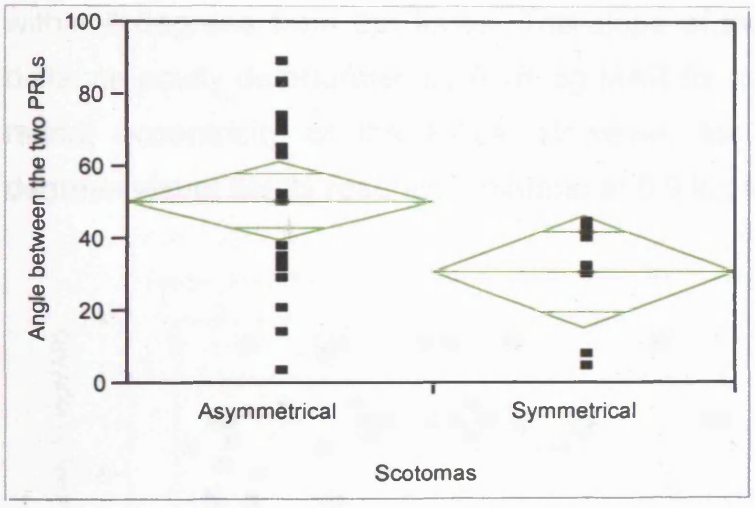


Figure 8.14. T- test analysis of the angle (in degrees) between the monocular PRLs in patients with symmetrical and asymmetrical scotomas. The line across each diamond represents the group mean. The vertical span of each diamond represents the 95% confidence interval for each group.

In order to assess retinal correspondence between the two PRLs, we calculated their horizontal and vertical distance separately. The range of the distance between them was 0.08° -12.5° (mean 4.4° ±3.3° SD) in the horizontal meridian and in the vertical meridian was 0.2° - 17.5° (mean 4.6° ±4.4° SD). Table 8.b in appendix 2 presents these distances for patients with both symmetrical and asymmetrical scotomas.

8.2.7. Can retinal eccentricity of monocular PRLs predict clinical performance?

The distances of the monocular PRLs from the normal fovea (DMFF) for all tested eyes were plotted against their distance visual acuity (Figure 8.15 and 8.16), contrast sensitivity (Figure 8.17 and 8.18) and MNREAD acuity (Figure 8.19 and 8.20), to assess whether retinal eccentricity could predict the responses to these clinical tests.

Regression analysis was used to investigate the relationship between retinal eccentricity and visual acuity. A straight line was not a good fit to the data and inspection of the residuals indicated that this relationship was nonlinear. Linear spline regression (Rubin et al. 2000) was performed with one inflection at 4 degrees eccentricity. Figure 8.15 demonstrates a linear relationship (r^2=0.26) between eccentricity of the PRLs and distance acuity when the PRL is located within 4 degrees from the fovea. The slope of this line is 0.18 indicating that distance acuity deteriorates by 0.18 log MAR for every unit change (degrees) in retinal eccentricity of the PRLs. However, for eccentricity greater than 4 degrees visual acuity reaches a plateau at 0.9 log MAR (r^2=0.028).

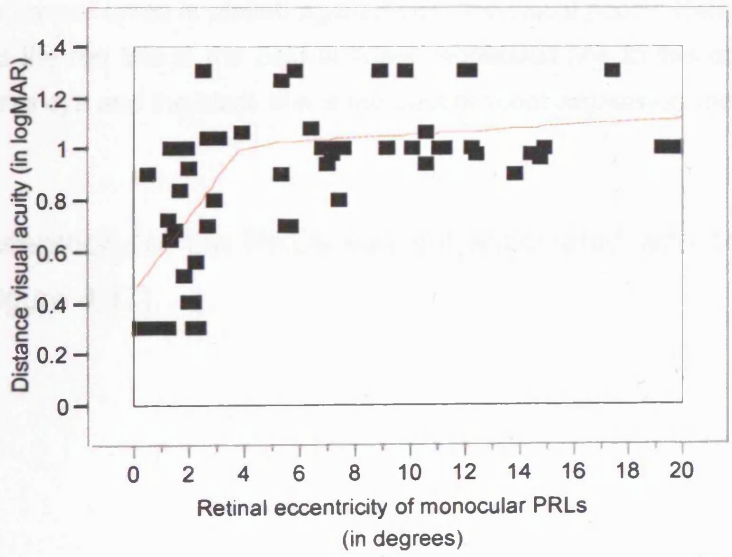


Figure 8.15. Retinal eccentricity (in degrees of visual angle) of monocular PRLs with respect to the normal fovea is plotted against distance visual acuity. The red line is the best fit line for the data.

We used further regression analyses to investigate the above correlation separately for the better and the worse eye for all patients (figure 8.16). Our

results showed that the eccentricity of the monocular PRL in the better eye was a very good predictor of distance acuity, while it was a poor predictor in the worse eye (r^2=0.52, p<0.0001 versus r^2=0.02, p=0.39). Using analysis of covariance we found that there was a significant difference between the slopes of the two regression lines (ANCOVA, P<0.0001).

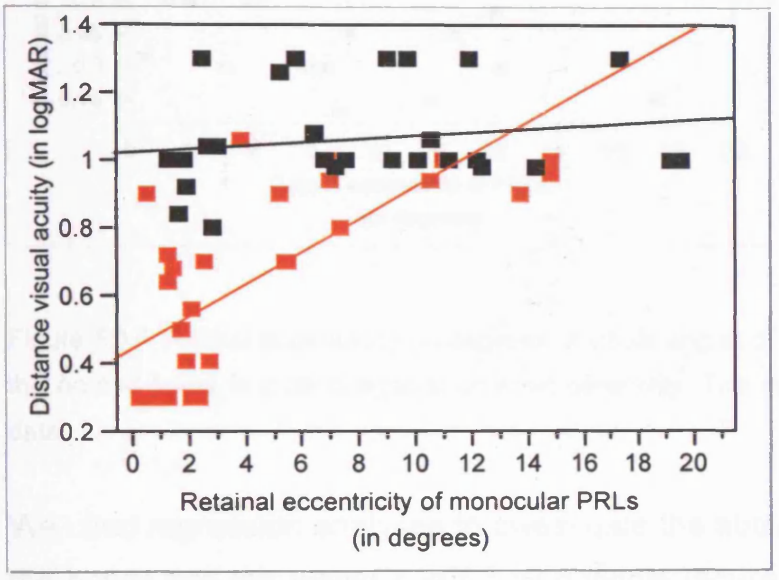


Figure 8.16. Retinal eccentricity (in degrees of visual angle) of monocular PRLs with respect to the normal fovea is plotted against distance visual acuity. Red squares represent the better eye and the red line is the best fit linear regression line to this data. Black squares represent the worse eye and the black line is the best fit linear regression line to this data.

Eccentricity of the PRLs was not associated with contrast sensitivity (r^2= 0.04) (Figure 8.17).

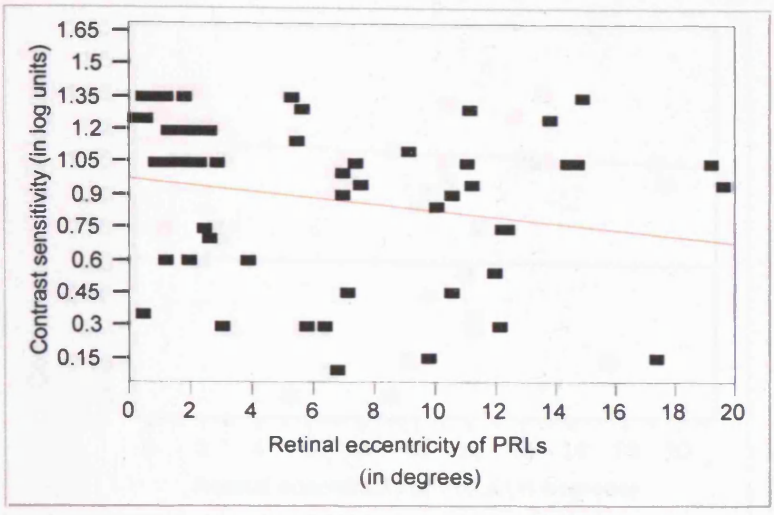


Figure 8.17. Retinal eccentricity (in degrees of visual angle) of monocular PRLs with respect to the normal fovea is plotted against contrast sensitivity. The red line is the best fit line for the data.

We used regression analyses to investigate the above correlation separately for the better and the worse eye for all patients (figure 8.18). Our results showed that the eccentricity of the monocular PRL in the better eye was a poor predictor of contrast sensitivity both in the better and in the worse eye (r^2=0.01, p=0.59 versus r^2=0.00, p=0.97). Although, in the majority of cases contrast sensitivity was better in the better eye compared to the worse eye for any given retinal eccentricity there was no significant difference between the slopes of the two regression lines (ANCOVA, P=0.82).

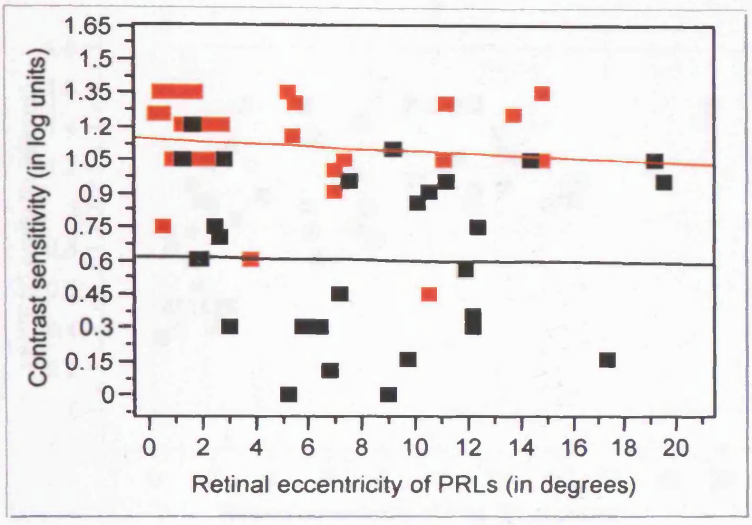


Figure 8.18. Retinal eccentricity (in degrees of visual angle) of monocular PRLs with respect to the normal fovea is plotted against contrast sensitivity. Red squares represent the better eye and the red line is the best fit linear regression line to this data. Black squares represent the worse eye and the black line is the best fit linear regression line to this data.

When PRL eccentricity was plotted against MNREAD acuity (Figure 8.19) a spline fit was used to analyse the data with one inflection again at 4 degrees eccentricity. A linear relationship was found between eccentricity of the PRLs and MNREAD acuity when the PRL is located within 4 degrees from the fovea (r^2= 0.14). The slope of this line is 0.13 indicating that MNREAD acuity deteriorates by 0.13 log MAR for every unit change (degrees) in retinal eccentricity of the PRLs. However, for eccentricity greater than 4 degrees MNREAD acuity the rate of change decreases (r^2= 0.13).

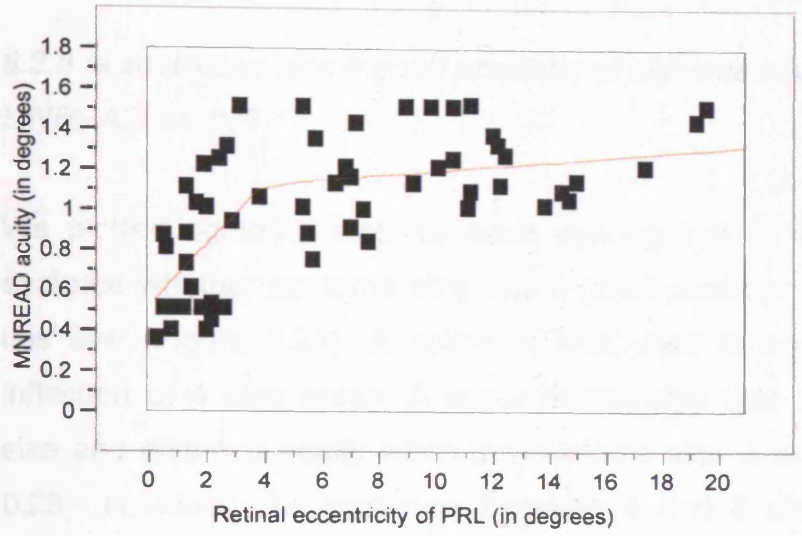


Figure 8.19. Retinal eccentricity (in degrees of visual angle) of monocular PRLs with respect to the normal fovea is plotted against MNREAD acuity. The red line is the best fit line for the data.

We used further regression analyses to investigate the above correlation separately for the better and the worse eye for all patients (figure 8.20). Our results showed that the eccentricity of the monocular PRL in the better eye was a very good predictor of MNREAD acuity, while it was a poor predictor in the worse eye (r^2=0.49, p<0.0001 versus r^2=0.17, p=0.02). There was no significant difference between the slopes of the two regression lines (ANCOVA, p=0.018).

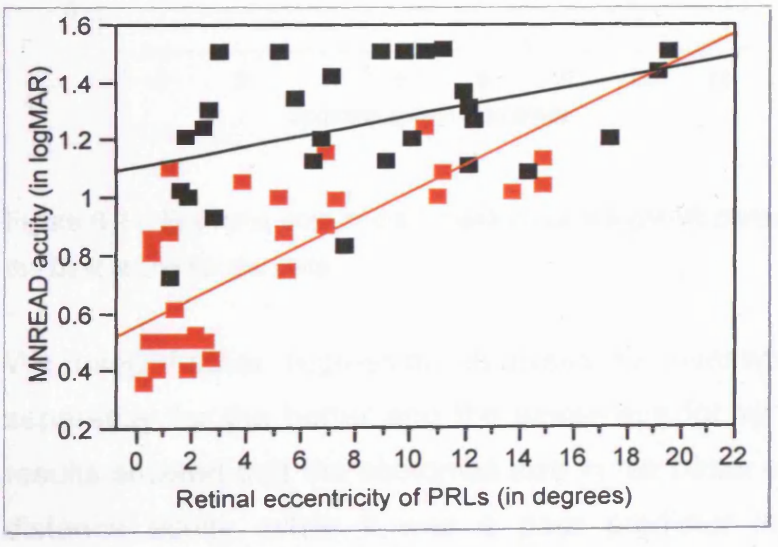


Figure 8.20. Retinal eccentricity (in degrees of visual angle) of monocular PRLs with respect to the normal fovea is plotted against MNREAD acuity. Red squares represent the better eye and the red line is the best fit linear regression line to this data. Black squares represent the worse eye and the black line is the best fit linear regression line to this data.

8.2.8 Is scotomas size a good predictor of distance acuity, contrast sensitivity or MNREAD acuity?

We plotted scotoma size for each eye against its distance visual acuity to evaluate whether scotoma size was a good predictor of the distance acuity for this eye (Figure 8.21). A spline fit was used to analyse the data with one inflection at 4 disc areas. A linear relationship was shown between scotoma size and distance acuity when the scotoma size is less than 4 disc areas (r^2= 0.26). However, for scotomas between 4 and 8 disc areas distance acuity reaches a plateau with only slight deterioration with further increase in scotoma size.

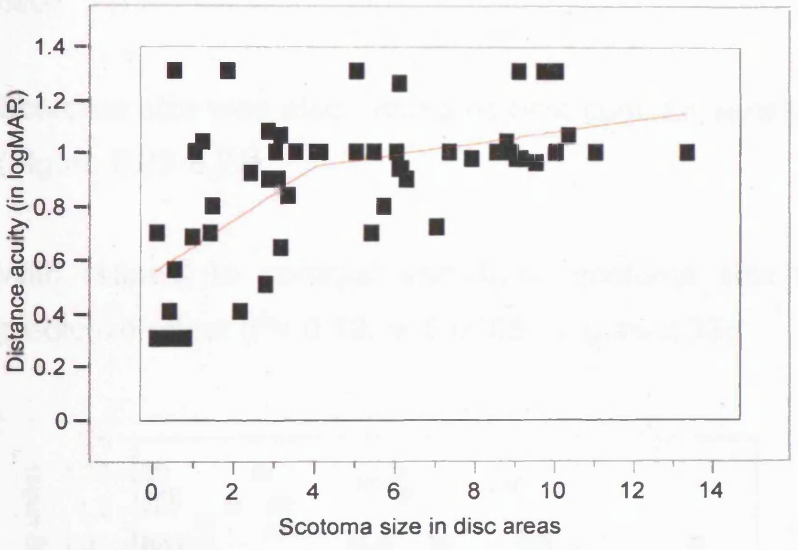


Figure 8.21. Scotoma size in disc areas against logMAR distance visual acuity. The red line is the best fit line for the data.

We used further regression analyses to investigate the above correlation separately for the better and the worse eye for all patients (figure 8.22). Our results showed that the scotomas size in the better eye was a good predictor of distance acuity, while it was a poor predictor in the worse eye (r^2=0.61, $p<0.0001$ versus r^2=0.02, $p=0.39$). There was a significant difference between the slopes of the two regression lines (ANCOVA, $p<0.0001$).

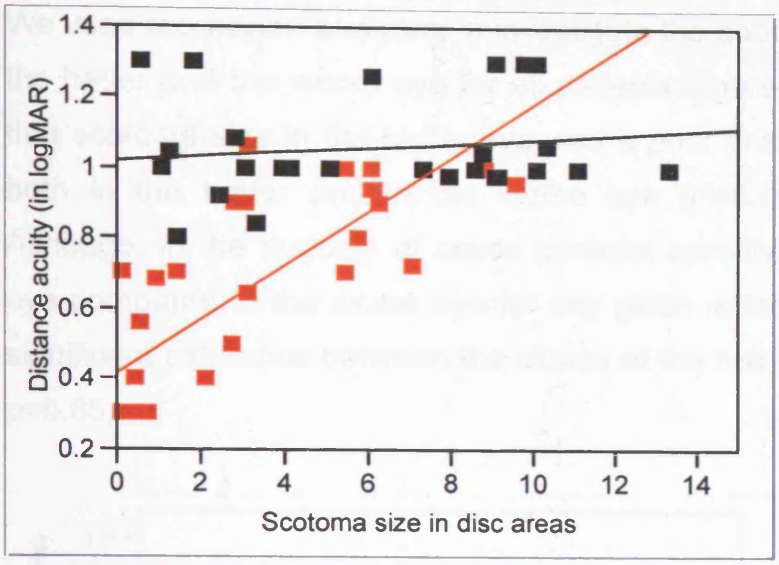


Figure 8.22. Scotoma size in disc areas is plotted against distance acuity. Red squares represent the better eye and the red line is the best fit linear regression line to this data. Black squares represent the worse eye and the black line is the best fit linear regression line to this data.

Scotoma size was also plotted against contrast sensitivity and MNREAD acuity (Figure 8.23-8.26).

With respect to contrast sensitivity, scotoma size was proven to have no predictive effect (r^2= 0.19, p=0.0005) (Figure 8.23).

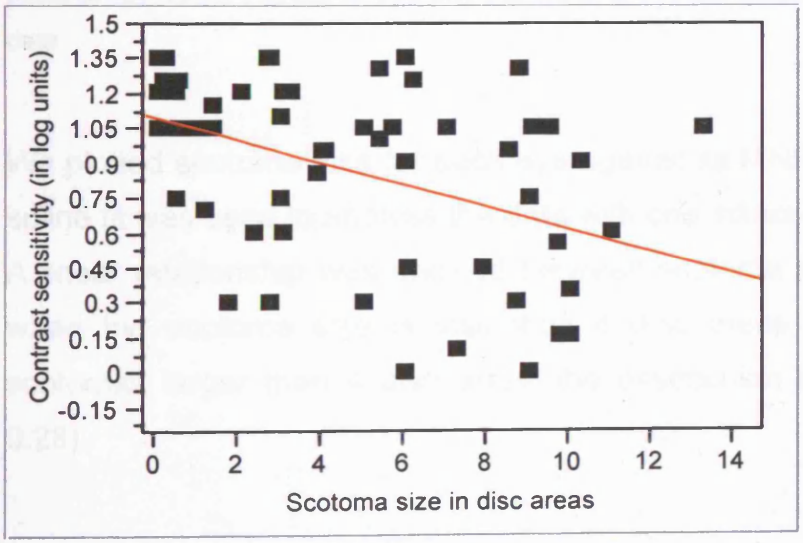


Figure 8.23. Scotoma size in disc areas against contrast sensitivity. The red line is the best fit linear regression line for the data.

We used regression analyses to investigate the above correlation separately for the better and the worse eye for all patients (figure 8.24). Our results showed that scotoma size in the better eye was a poor predictor of contrast sensitivity both in the better and in the worse eye (r^2=0.05, p=0.20 for both eyes). Although, in the majority of cases contrast sensitivity was better in the better eye compared to the worse eye for any given retinal eccentricity there was no significant difference between the slopes of the two regression lines (ANCOVA, p=0.85).

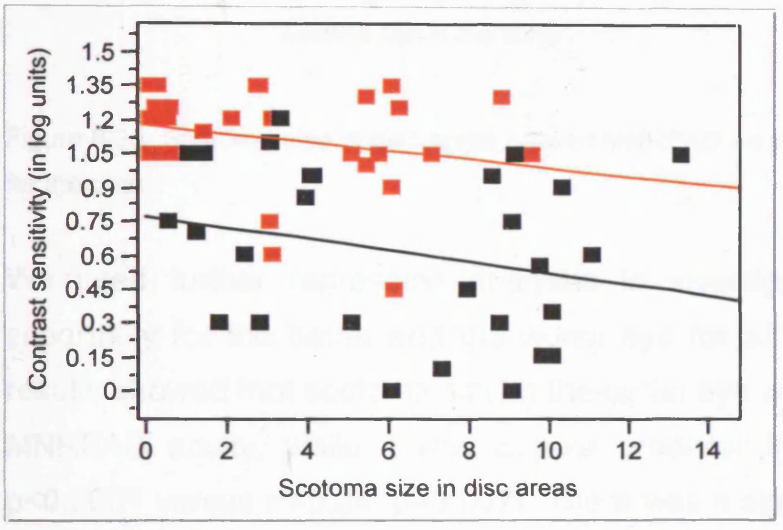


Figure 8.24. Scotoma size in disc areas is plotted against contrast sensitivity. Red squares represent the better eye and the red line is the best fit linear regression line to this data. Black squares represent the worse eye and the black line is the best fit linear regression line to this data.

We plotted scotoma size for each eye against its MNREAD (Figure 8.25) and a spline fit was used to analyse the data with one inflection at 4 disc areas.
A linear relationship was showed between scotoma size and MNREAD acuity when the scotoma size is less than 4 disc areas (r^2= 0.33). However, for scotomas larger than 4 disc areas the association is marginally weaker (r^2= 0.28).

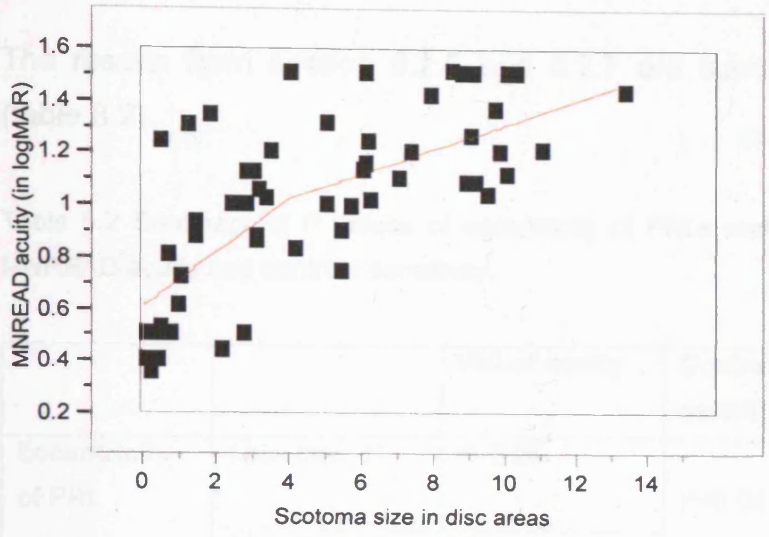


Figure 8.25. Scotoma size in disc areas against MNREAD acuity. The red line is the best fit line for the data.

We used further regression analyses to investigate the above correlation separately for the better and the worse eye for all patients (figure 8.26). Our results showed that scotoma size in the better eye was a very good predictor of MNREAD acuity, while it was a poor predictor in the worse eye (r^2=0.68, $p<0.0001$ versus r^2=0.24, $p=0.007$). There was a significant difference between the slopes of the two regression lines (ANCOVA, $p=0.0003$).

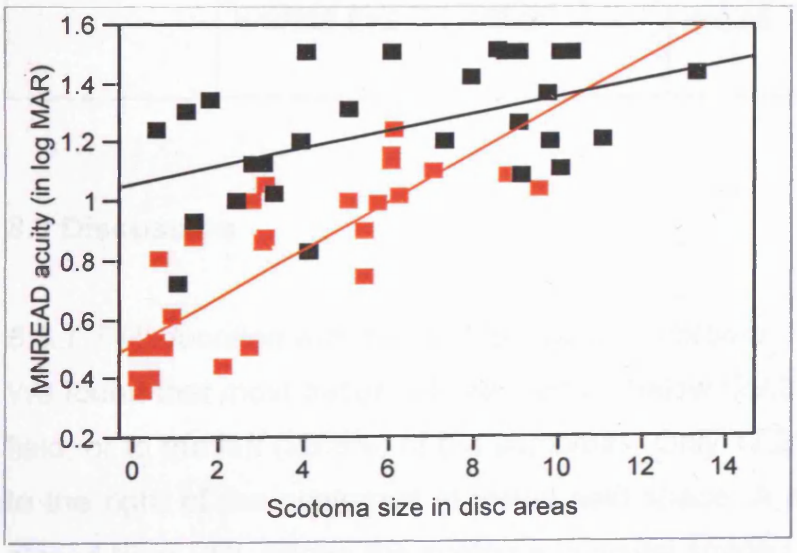


Figure 8.26. Scotoma size in disc areas is plotted against MNREAD acuity. Red squares represent the better eye and the red line is the best fit linear regression line to this data. Black squares represent the worse eye and the black line is the best fit linear regression line to this data.

The results from section 8.2.6 and 8.2.7 are summarized in the table below (table 8.2).

Table 8.2 Summary of r^2 values of eccentricity of PRLs and scotoma size for distance and MNREAD acuity and contrast sensitivity.

		Visual acuity	Contrast sensitivity	MNREAD acuity
Eccentricity of PRL	*Less than 4°*	r^2=0.26	r^2=0.04	r^2=0.14
	More than 4°	Plateau		r^2=0.13
Scotoma size in disc areas	*Less than 4 DA*	r^2=0.26	r^2=0.14	r^2=0.33
	More than 4 DA	Plateau		r^2=0.28
Eccentricity of PRL	*BETTER EYE*	r^2=0.52	r^2=0.01	r^2=0.49
	WORSE EYE	r^2=0.02	r^2=0.00	r^2=0.17
Scotoma size in disc areas	*BETTER EYE*	r^2=0.61	r^2=0.05	r^2=0.68
	WORSE EYE	r^2=0.02	r^2=0.05	r^2=0.24

8.3 Discussion

8.3.1. PRL location with respect to macular scotoma

We found that most patients fixated either below (29.3%) the scotomas in visual field, or to the left (25.8%) of the scotomas. Only 17.2% of patients used a PRL to the right of the scotomas in visual field space. A minority of tested patients placed their PRL above the scotoma in visual space (10.3%). Furthermore, few patients (3%) fixated with their better eye on a normal central retinal area surrounded by multiple small scotomatous areas. 12% of patients placed their PRL mainly in their worse eye on a possible island of vision within the scotomatous area.

Most of the previous studies indicated that AMD patients tend to fixate mainly below (percentages vary across the studies from 86% to 15%) and to the left (from 63% to 16%) of their scotomas in visual space (White and Bedell 1990; Guez et al. 1993; Sunness et al. 1996; Fletcher and Schuchard 1997; Nilsson et al. 1998; Fletcher et al. 1999). We found that most of our patients also fixated below and to the left of the scotomas and our recorded percentages fell within the reported values and therefore, our results are in accordance with previous published work.

Previous literature attempted to explain the advantages of fixation in the upper retina (lower visual field). It has been noted that retinal cell density is slightly higher in this area (Anderson et al. 1991; Curcio et al. 2000). Moreover, reading seems faster (Petre et al. 2000) in the upper retina (lower visual field) as in that way the retina area used for fixation is not interrupted by the presence of the scotoma and the subsequent lines to be read are all visible.

In our study only marginally more patients used a horizontally located PRL with respect to the scotoma (right or left of the scotomas) than a vertically located PRL (above or below the scotomas); 25 patients fixated in the horizontal meridian versus 23, who fixated in the vertical meridian. Sunness et al (Sunness et al. 1996) suggested that using a horizontally located PRL in cases of geographic atrophy is more likely to be attributed to the horseshoe appearance of the earlier lesion that allows a horizontal PRL to have more close proximity to the fovea. It is very interesting though that these patients tend to read towards their scotomas instead of away from them (using more often a PRL located to the left of the scotoma than to the right in visual space) (see section 1.3).

Most AMD patients (except from two patients; recordings from three eyes) placed their PRL very close to the borders of the scotomas in accordance with previous reports (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999) and in contrast to juvenile macular diseases where patients tend to fixate further away from the scotomas edges (Timberlake et al. 1986; Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999).

In AMD patients in general, fixation locus seemed to shift to the site of retina closest to the fovea (Tezel et al. 1996). However, Sunness et al (Sunness et al. 1996) suggested that the preference for fixation to the right of the scotomas in visual space overrides proximity to the fovea. In addition, in the same study, they did not manage to explain according to the foveal position the second most selected preference for fixation below the scotomas.

8.3.2. Symmetry/ Asymmetry of macular scotomas due to AMD

All groups investigating symmetry of retinal lesions due to ARM (including patients with choroidal neovascular membrane, retinal pigment epithelium tears and disciform scars) (Chuang and Bird 1988; Lavin et al. 1991; Wang et al. 1998) concluded that there were high rates of symmetric manifestations of AMD between the two eyes. However, in our study, when scotomas sizes were measured and compared between the two eyes, there was no significant correlation. In particular, only one third of them had symmetrical scotomas (interocular difference ≥ 1 disc areas) while the remaining had non-symmetrical scotomas. AMD is a bilateral eye condition but both eyes are not affected simultaneously so most of the patients experience some degree of asymmetry in macular lesions during the course of the disease (Gregor et al. 1977; Strahlman et al. 1983; Bressler et al. 1990; Roy and Kaiser Kupfer 1990; Macular Photocoagulation Study Group 1993a). However, as the major determinant of ARM is age (Sperduto and Seigel 1980; Klein et al. 1992; Vingerling et al. 1995), it is expected that bilateral involvement will be increased with age.

8.3.3. Scotoma size and PRL location

Fixation locus seemed to shift to the site of retina closest to the fovea. Previous work has shown that AMD patients fixate very close to the borders of the scotomas (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999). As a result of this macular scotoma size should be a good predictor of retinal eccentricity of PRL location. Indeed, in this study it was found to be a good predictor of retinal eccentricity of the monocular PRL with respect to the normal fovea (r^2= 0.49). Some outliers were patients that fixated further away from the borders of the absolute scotomas. Possible further anatomic abnormalities not

causing absolute scotomas and therefore, not mapped with microperimetry, could shift the PRL further away and could explain this behaviour. Furthermore, some patients fixated within an island of normal retinal function within the scotomatous area and thus, the distance of their PRL to the fovea did not show a good correlation with the scotomas size. Although scotoma size was a better predictor of the eccentricity of the PRLs' position in the better eye compared with the worse eye there was no significant difference between these two regression lines.

8.3.4. Interocular s*ymmetry and asymmetry of macular scotomas and difference in eccentricity of PRLs between the two eyes and effect on retinal correspondence.*

There is a relatively good correlation (r= 0.61) between interocular differences in scotomas size and difference in eccentricity of monocular fixation locus between the two eyes. One reason that can explain the lack of a better correlation is the fact that despite symmetrical scotomas sizes a difference in foveal sparing in the two eyes can affect PRL position (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999). Moreover, patients with geographic atrophy initially develop a horseshoe appearance of the atrophic lesion. This can therefore give rise to a fixation area with a very close proximity to the fovea despite the presence of an absolute scotoma. Furthermore, lesions may look symmetrical, but the presence of additional anatomic abnormalities not mapped as 'absolute' scotomas can cause further shift of the PRL to more peripheral locations in one eye and not to the other.

Patients who had symmetrical scotomas showed significantly smaller distances (and therefore, similar retinal eccentricities) between their monocular PRLs compared to patients with asymmetrical scotomas, which is in accordance with hypothesis 1. If we define retinal corresponding points as the points in the two eyes that have the same horizontal and vertical distances from the two foveolas, and therefore zero distance between them, then obviously none of our patients satisfied this criterion. As this is the theoretical definition of retinal correspondence it is rather unrealistic in practice. Therefore, we considered corresponding retinal points as the ones which, when simultaneously stimulated give rise to the percept of a single object (Millidot, Dictionary of Optometry).

Panum's area defines the area over which single vision can be obtained. Its extent though is rather narrow (narrowest at the fovea with a width of 6 to 10 minutes, which increases towards the periphery at a rate of 1 to 2 min of arc per degree of visual field eccentricity to reach to 30 to 40 minutes at 12°) (von Noorden and Campos 2002) (see section 2.1). None of our patients used monocular PRLs in the two eyes that fell within Panum's area (see tables 8a and 8b, appendix 2). Possible measurement errors could account for these results. We listed the possible sources of measurement errors in Table 8.3 below.

Table 8.3. Sources of measurement errors during calculation of distances between monocular PRLs (horizontal and vertical meridian).

Source of measurement errors		
Prediction of centre of blind spot on SLO images (section 6.2.2)	Width of 95% CL	0.5° horizontally 0.6° vertically
Distance of the fovea to the centre of the blind spot (table 6.2)	Width of 95% CL	2.4° horizontally 0.8° vertically

In order to compare our results with this table the distances between the two PRLs in the horizontal and the vertical meridians were taken into account. We looked at these differences for the patients with symmetrical scotomas (see table 8.b, appendix 2) and we compared them with the total measurement error distances from the above table (overall distances: 2.9° horizontally and 1.4° vertically). Six patients (subject no 11, 16, 18, 19, 25, and 30) demonstrated distances that fell within the measurement error areas in the horizontal meridian and five patients (subject no 14, 16, 18, 19 and 25) showed distances that fell within the measurement error area in the vertical meridian. However, if we take into consideration both meridians only in three patients (subjects no 16, 18 and 25) the distances between the two monocular PRLs could be attributed to measurement errors.

For the patients with asymmetrical scotomas, five patients (subject no 7, 26, 27, 28, 29) demonstrated distances that fell within the measurement error areas in the horizontal meridian but only two patients (subject no 13 and 28) in the vertical meridian. When both meridians were taken into account, it was evident that the distances between the two monocular PRLs could be explained from measurement errors only in one patient (subject no 28). In all the cases that the distances between the monocular PRLs could not be explained due to Panum's area and measurement errors it was hypothesized that these patients had non corresponding monocular PRLs.

Thus, we have shown that the monocular PRLs seem to fall on more corresponding retinal areas in patients with symmetrical scotomas compared to patients with asymmetrical scotomas which is in agreement with this part of hypothesis 1.

8.3.5. Distance visual acuity, contrast sensitivity and MNREAD acuity and retinal eccentricity of PRL position

Retinal eccentricity of PRL position and scotoma size was a relatively good predictor for distance acuity (r^2= 0.26 in both cases) when the PRL was located within 4 degrees from the fovea and the scotoma size was less than 4 disc areas. For eccentricity greater than 4 degrees visual acuity reaches a plateau at 0.9 logMAR, while for scotomas greater than 4 disc areas distance acuity reaches a plateau with only slight deterioration with further increase in scotoma size.

In normal subjects visual acuity decreases sharply with increased eccentricity. Even 1 degree away from the fovea a reduction to about 60% of maximum has been documented (Weymouth et al. 1928). Wertheim (Wertheim 1980) reported that visual acuity was reduced to 6/12 at 2.5 degrees and to 6/30 at 10 degrees in the horizontal meridian, nasally to the fovea. He also demonstrated that it decreases more sharply below and above the fovea, and therefore, the lines connecting points of equal visual acuity are elliptic, in parallel with the outer margins of the visual field. For a given angle of eccentricity the temporal field seems to exhibit better acuity levels compared to the nasal field of view (Adler

1987). Ludvigh (Ludvigh 1941) gave more detailed information on extrafoveal acuity up to 10 degrees eccentricity (figure 8.27).

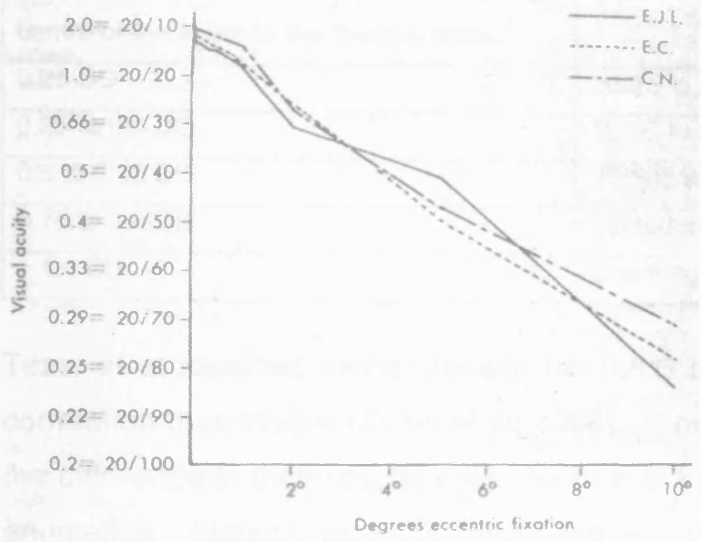


Figure 8.27 Visual acuity plotted against retinal eccentricities (in degrees of visual angle) for three normal subjects. Ludvigh E: 1941. Arch Ophthalmol

According to figure 8.27, at a retinal eccentricity of 4 degrees normal subjects have a visual acuity of 0.5logMAR, while in our study for AMD patients this was measured at 0.9 log MAR. In accordance with our results previous papers have documented that visual acuity in AMD patients is worse at their fixation locus than was expected from normal data for that given eccentricity (Brown et al. 1984; Rees et al. 2004). According to previous results on normal patients (Ludvigh 1941) retinal eccentricity of 4 degrees in normal subjects has visual acuity of 0.5 logMAR, while in our study for AMD patients is measured only 0.9 logMAR (figure 8.15). However, in the correlation in the better eye visual acuity is 0.6 logMAR which is very close to normal values.

Weiter et al. (Weiter et al. 1984) also reported that recorded visual acuity in AMD patients is worsened as the fixation point moved away from the fovea and he described a high correlation between them (table 8.4).

Table 8.4 Distance in disc diameter (DD) from the centre of the fovea to the fixation locus and recorded best visual acuity (in logMAR) at this locus. Weiter et al. 1984 Ann Ophthalmol

Distance in disc diameter (DD) from the centre of the fovea to the fixation locus	Best visual acuity in logMAR
0.25 DD	20/25 to 20/50
0.25 to 0.5 DD	20/50 to 20/100
0.5 to 0.75 DD	20/100 to 20/200
0.75 to 1.0 DD	20/200 to 20/400
> 1.0 DD	Counting fingers

Tezel et al reported similar results (r= 0.81) although they showed a weaker correlation than Weiter (Tezel et al. 1996). They suggested that one reason that the difference in their results could be due to the presence of multiple anatomic anomalies (detachment of the retinal pigment epithelium, subretinal haemorrhage, RPE atrophy) that could further affect the visual acuity at the fixation locus.

Moreover, it has been suggested that even when the PRL is at the edge of the scotoma visual acuity is not always proportional to the eccentricity of the fixation locus. A possible explanation given by Guez et al (Guez et al. 1993) seems to be that the patient prefers a less eccentric position for the pseudo-fovea, in a part of the retina which may not be completely healthy, rather than going further into peripheral retina with better acuity. The same observation was also reported by White and Bedell (White and Bedell 1990).

As was mentioned earlier, Sunness and others (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999) suggested that the preference for fixation to the right of the scotoma in visual space was overridden by the consideration for proximity to the fovea. One might think that the PRL used during SLO recordings is not the same as the one used to measure acuity on the clinical test (ETDRS chart) and this could explain the weak correlation. However, the visual acuity measured with the SLO and ETDRS chart showed minimal difference (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999), which was suggestive of patients using the same fixation to perform the clinical test and the SLO task.

Regarding scotoma size and visual acuity the above authors also observed that although there was high symmetry of retinal lesions (geographic atrophy) between the two eyes, there was a large variation in the visual acuity between the better and the worse eyes. They attributed this to a different degree of foveal sparing between the two eyes and / or to a possible suboptimal use of the remaining functional retina in the worse eye. The fact that the ability to use the remaining retina in the presence of a central scotoma can be reduced in the worse eyes of patients with bilateral advanced geographic atrophy has also been reported (Sunness et al. 1999). In support of these hypotheses is the fact that an improvement in the visual acuity in the worse seeing eye can be observed when the better seeing eye begins to deteriorate (Sunness et al. 2000).

Regarding contrast sensitivity, we found that eccentricity of the PRLs and scotoma size had no predictive value (r^2= 0.04 and r^2= 0.14 respectively). Although the correlation was better for the better eye compared to the worse eye neither of them was reached good predictive values.

We reported that retinal eccentricity of PRL position was a relatively weak predictor for MNREAD acuity for any eccentricities (when less than 4 degrees: r^2= 0.14 and when more than 4 degrees: r^2= 0.13). When the scotoma size was less than 4 disc areas it was a relatively good predictor of MNREAD acuity (r^2= 0.33). However, for scotomas larger than 4 disc areas the association was weaker (r^2= 0.28). Ergun et al. (Ergun et al. 2003) reported a similar correlation between reading acuity and absolute scotoma size (r=0.52 versus our results r=0.57), using a similar test for measuring reading acuity (Radner Lesetest). However, the predictive value of the eccentricity of the PRL and scotoma size was good for MNREAD acuity only for the better eye (r^2=0.49 and r^2=0.68 respectively for the better eye; r^2=0.17 and r^2=0.24 respectively for the worse eye). We found significant difference in the above correlations between the better and the worse eye for both scotomas size and eccentricity of the PRL.

8.4 Conclusions

Most of AMD patients fixated below or to the left of their scotomas in visual space. Most AMD patients fixated very close to the borders of the scotomas. As a result of this macular scotoma size was a good predictor of retinal eccentricity of PRL location.

Overall, only one third of our patients had symmetrical scotomas. There was a significant correlation between interocular differences in scotoma size and difference in eccentricity of monocular fixation locus between the two eyes. A difference in foveal sparing in the two eyes and the presence of additional anatomic abnormalities not mapped as 'absolute' scotomas may have prevented a better correlation.

Patients with symmetrical scotomas showed significantly smaller distances between their monocular PRLs compared to patients with asymmetrical scotomas and therefore were using PRLs with similar retinal eccentricities. Therefore, the monocular PRLs seemed to fall on more corresponding retinal areas in patients with symmetrical scotomas compared to patients with asymmetrical correspondence which is in agreement with hypothesis 1.

Scotoma size was a better predictor of the eccentricity of the PRLs' position in the better eye compared with the worse eye but there was no significant difference between them.

Retinal eccentricity of PRL position and scotomas size was a relatively good predictor of distance acuity when the PRL was located within 4 degrees from the fovea and the scotoma size was less than 4 disc areas although recorded acuities were worse when compared with normal subjects at similar retinal eccentricities. Moreover, both of the above measurements were good predictors of distance acuity only in the better eye and not in the worse.

Eccentricity of the PRLs and scotoma size were weak predictors of contrast sensitivity. Although, in most cases both of the above measurements were

better predictors in the better eye compared to the worse eye for any given retinal eccentricity, there was no significant difference between them.

Overall, scotoma size was a relatively good predictor of MNREAD acuity but eccentricity of PRL was a weak predictor for MNREAD acuity for any retinal eccentricities. Moreover, both of the above measurements were good predictors of MNREAD acuity only in the better eye and not in the worse.

CHAPTER 9

BINOCULAR VIEWING CONDITIONS: PRLs AND CLINICAL PERFORMANCE

As SLO recordings provide only monocular viewing data an infrared eyetracker was used to acquire binocular data during a fixation task. Since some video eye trackers allow recording under natural viewing conditions (as there is no requirement for head or chin support), they often offer a practical alternative to the SLO. The eyetracker used in this study measures gaze position by detecting the location of the pupil centre, indirectly indicating the location of the PRL on the retina.

Chapter 9 is divided in four main sections. In the first section (9.1.1) changes in gaze position under monocular versus binocular viewing conditions are recorded in AMD patients by means of an infrared eyetracker. These data provide indirect information about the retinal locus used for fixation in each eye under both viewing conditions. In section 9.1.2 the main question is whether patients used the same or different PRL to fixate under monocular versus binocular viewing conditions during a simple fixation task. Furthermore, evaluation of fixation stability and the presence of multiple PRLs during monocular and binocular viewing were also evaluated. The next section (9.1.3) describes a method to predict the binocular fixation loci on SLO infrared images. The distances of these loci from the fovea are also measured and the retinal correspondence of the binocular PRLs for both eyes is assessed. Finally, we will investigate whether binocular performance in clinical measurements such as distance and MNREAD acuity, and contrast sensitivity, and/or ability for fusion, is affected by the symmetry of macular scotomas (section 9.1.4).

Therefore, in this chapter hypotheses 2, 3, 4 and 5 will be explored (section 4.2).

According to hypothesis 2:
In patients with symmetrical scotomas no shift in gaze position is expected from monocular to binocular viewing. Therefore, patients are expected to use the same PRLs under both viewing conditions in both eyes. However, patients with

asymmetrical scotomas are expected to use different PRLs under binocular versus monocular viewing in the worse eye. A shift in the PRL locus is expected in the worse eye under binocular versus monocular viewing conditions.

Hypothesis 3 predicts that:
AMD patients will exhibit PRLs under binocular viewing conditions with similar retinal eccentricities between the two eyes. These PRLs are likely to fall on corresponding retinal areas in the two eyes. No difference is expected in patients with symmetrical versus asymmetrical scotomas with respect to retinal correspondence of binocular PRLs.

Hypothesis 4 states that:
Fusion is expected to be preserved in patients with corresponding PRLs that fall outside the scotomas. Therefore, fusion should be preserved in patients with symmetrical scotomas but not in cases with asymmetrical scotomas.

Hypothesis 5 predicts that:
Clinical performance is expected to be superior under binocular viewing conditions compared with the performance using the better eye only in patients with symmetric scotomas. Clinical performance is expected to be equal or worse under binocular viewing conditions compared with the performance using the better eye only in patients with asymmetric scotomas.

9.1. Methods

Thirty patients with bilateral AMD and ten normal subjects were included in the study. The mean of age of AMD subjects was 79.8± 5.6 SD years and of normals 75.8 ± 4.9 SD years.

9.1.1. Eye tracking

The subject was seated 50 cm away from the computer monitor (21" Trinitron GDM-F500R, Sony, Japan) during the test and wore a spectacle correction for this distance (+2.00 dioptres in addition to the distance correction). The background screen luminance was 125cd/m^2, screen resolution was 1024x768 pixels and the refresh rate was 70 Hz.

Calibration

Calibration of the instrument was performed monocularly with each eye using manufacturer's algorithms before initiation of data recording. The fellow eye was occluded. The calibration target was a black dot with a total diameter of 2.2° and a central white opening of 0.4° diameter. Calibration was performed using a 5-point grid. The target was first displayed in the centre then appeared randomly at the top, bottom, left edge, and right edge of the monitor. The patient was instructed to move his eyes so that the central opening of the fixation target was best seen; and when the patient verified that this had been achieved, the fixation was registered by the system. Only trials where the calibration was categorised as 'good' by the Eyelink software were included. Calibration was described as 'good' when at least minimal nonlinearity existed when fixating different target positions (maximum ratio of gains=1.5:1 horizontally, 3:1 vertically) (Crossland et al. 2004 and 2004a). Drift correction and validation were performed using the algorithms provided for this purpose then the recording phase was initiated.

Recording phase

There were two separate trials during the recording phase. During the first trial the patient was asked to fixate the target monocularly. The fixation target was displayed centrally on the monitor. It was presented for 30 seconds and the subject was asked to keep fixation as stable as possible during that time. Before the second trial began the occluder was removed and the patient was asked to fixate the same target with both eyes for 30 seconds. Eye position was recorded only from the eye used for calibration of the instrument. Data from both trials were stored for later analysis. The calibration and the same recording procedures were then repeated for the other eye.

9.1.2. Data analysis of eyetracker data

A programme to analyse raw SMI data using software written in Matlab and S-plus was developed by Crossland et al (Crossland and Rubin 2002; Crossland et al. 2004a). Data were disregarded during the first second of recordings (to ensure that the patients had accurately found the target on the screen), 0.25 sec before and 0.5 sec after the start of a blink and where eye movements

exceeded 30° /sec (during saccades). To ensure that not too much data were removed, trials in which less than 40% of the recordings remained were discarded. The rest of the trials were accepted for further analysis.

9.1.2.1. Bivariate contour ellipse area (BCEA)

Based on the distribution of gaze position in a scatter plot the bivariate contour ellipse area (BCEA) was calculated in min of arc^2 using an equation first described by Steinman (Steinmann 1965) but used by many others investigators (Nachmias and Kocher 1970; Timberlake et al. 1986; Schuchard and Raasch 1992; Culham et al. 1993). This is an ellipse, which describes the portion of retinal surface where the centre of the target was imaged for P% of the time. Different P values have been used in the past by other researchers such as 63.2% (Steinmann 1965), 68% (Nachmias 1959; Culham et al. 1993) or 95% (Schuchard and Raasch 1992). We used a P value of 68% for this study to be consistent with previous work in our lab (Culham et al. 1993; Crossland and Rubin 2002). As smaller BCEAs indicate more stable fixation their calculation enabled us to assess and quantify fixation stability for each eye under both viewing conditions (monocular and binocular).

Regression analyses were used to investigate whether distance and MNREAD acuity, contrast sensitivity, scotoma size and retinal eccentricity of the PRL for each eye were good predictors of the size of the BCEAs.

9.1.2.2. Number of PRLs

The use of multiple PRLs has already been described in the literature (Whittaker et al. 1988; Lei and Schuchard 1997; Duret et al. 1999; Deruaz et al. 2002; Deruaz et al. 2004), even during a simple fixation task (Whittaker et al. 1988; Crossland et al. 2004a). Therefore, analyses using a kernel density estimation procedure (KDE) were applied to determine the number of PRLs used during the task. This technique has been described elsewhere in detail (Crossland et al. 2004a) and it provides the most objective method of determining the numbers of clusters of fixation within a set of bivariate data that is currently available. The parameters of each PRL such as the mean x and y positions (in pixels), and an estimation of the proportion of the data which fell into each locus were determined during monocular and binocular recordings. If

less than 20% of the data fell into one locus then this PRL was disregarded, in accordance with prior definitions of a PRL (Whittaker et al. 1988). Moreover, if the difference in the mean x and y position of two or more PRLs was less than 3° these PRLs were treated as one, again following Whittaker et al (Whittaker et al. 1988). However, in other reports multiple PRLs were identified only if the patients were using retinal areas to fixate the target that were located at different retinal quadrants (Lei and Schuchard 1997; Duret et al. 1999).

9.1.2.3. Shift in gaze position

A mean x- and y- position of the centre of the ellipse was also calculated that corresponded to the mean gaze position during the task under both viewing conditions. Any difference of the calculated mean x and y data between monocular and binocular viewing conditions was calculated. All the data were converted to degrees of visual angle for further evaluation. For the viewing distance of 50cm, 1° of visual angle corresponds to ~23 pixels on the monitor screen.

9.1.2.4. Normal data recordings

Ten normal subjects performed the same test. Their data were used to decide when the changes in gaze position during monocular versus binocular recordings were indicative of a different retinal locus used for fixation. The value of the mean ± 2 SD of their measurements was considered the cut off point of the normal changes in gaze position for this particular task.

Two consecutive eye-tracking measurements were performed by five AMD patients and eight normal subjects to measure the repeatability of the procedure.

9.1.3. Binocular fixation locus

9.1.3.1. Retinal location of binocular PRLs

As mentioned in chapter 6 (section 6.1.5) AMD patients could not perform the mapping of the blind spot test and therefore, we did not manage to demonstrate that they were using the same PRL to fixate the target on the SLO and the eyetracker. However, we excluded from this study patients that exhibited

multiple PRLs during eyetracker recordings under monocular and/or binocular viewing using the method developed by Crossland et al. (Crossland et al. 2004a). In that respect, patients that were using a single PRL to fixate the target on the computer monitor using the eyetracker were assumed to use the same PRL to fixate during SLO recordings. In addition, every effort was made to match the experimental conditions when using the two devices (properties of the target, background luminance, etc – see section 5.5).

Based on the above assumption that patients were using the same PRL to fixate the target under monocular viewing conditions during recording on the SLO and the eyetracker, the shift of position of gaze recorded by the eyetracker from monocular to binocular viewing conditions was 'added' to the monocular PRL position on the SLO image. The resultant retinal locus was defined as the binocular PRL for that eye.

9.1.3.2. Distance of binocular fixation locus from 'fovea'

The distance between binocular fixation locus and the fovea was calculated for both eyes for all tested subjects in degrees of visual angle based on the SLO images in a similar way as in section 8.1.4. We referred to this distance as DBFF (distance from binocular fixation to fovea) and it was defined as the vector sum of the horizontal and vertical difference between the fovea and the binocular PRL.

9.1.3.3. Assessment of retinal correspondence of binocular PRLs

Polar coordinates were used to describe the distance between the binocular fixation loci used by the two eyes by calculating the magnitude of the distance (the vector sum of the horizontal and vertical difference between the two loci) and the angle between them (as in section 8.1.6).

Subsequently, these distances were calculated separately in the horizontal meridian and in the vertical meridian in order to assess retinal correspondence of the binocular PRLs for patients with symmetrical and asymmetrical scotomas.

9.1.4. Binocular performance in clinical tests and its relationship with the interocular symmetry of macular scotomas

We assessed whether binocular performance on clinical tests (distance acuity, contrast sensitivity and MNREAD acuity) and ability for fusion was affected by the presence of symmetrical or asymmetrical macular scotomas (combination of results from chapter 7, 8 and 9).

9.2. Results

9.2.1. Fixation stability during monocular and binocular recordings

The results from the recordings under monocular and binocular conditions for both eyes using the infrared eyetracker are presented in table 9.a in appendix 2.

As the distribution of the recordings did not follow a normal distribution we calculated the median BCEA values and the range for each recording. These results are presented in table 9.1. Subject 23 had very large BCEA compared to the rest of the subjects and as will be demonstrated later he was using multiple PRLs during the fixation task. Therefore, he was excluded from table 9.1. A Wilcoxon test was used to compare monocular and binocular BCEAs for the better and worse eye.

Table 9.1. Median BCEA values and the range for monocular and binocular recording for both eyes for all tested AMD subjects. Results from the Wilcoxon test are presented in the last column of the table.

	Monocular recordings	**Binocular recordings**	*Wilcoxon test*
Better eye	median :7943 (range:1120-74346)	median: 8503 (range:851-145747)	p=0.65
Worse eye	median: 34860 (1436-113770)	median: 19933 (range:747-217966)	p>0.05

As BCEA values were not normally distributed a log transformation was performed to normalise them and consequently, regression analysis was used to investigate the correlation between the BCEAs in both eyes under binocular

viewing conditions (figure 9.1). There was, indeed, a good correlation between them (r=0.76).

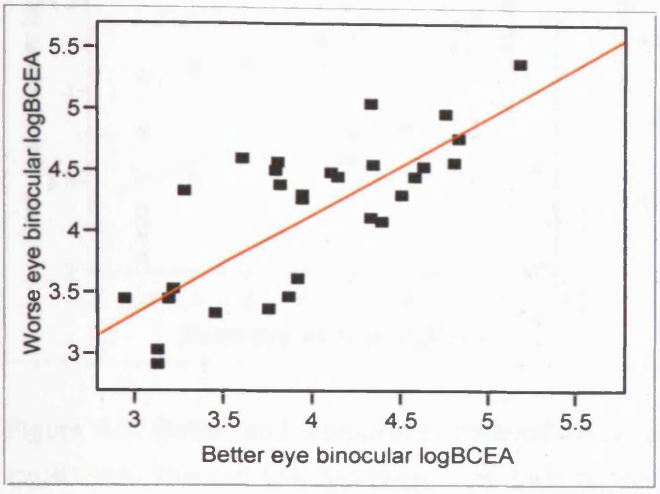


Figure 9.1 Better eye BCEA (in min of arc²) is plotted against worse eye BCEA (both under binocular recording conditions). The red line represents the best fit linear regression line to the data.

The size of the monocular BCEAs is plotted against distance visual acuity, contrast sensitivity and MNREAD acuity for each eye in figures 9.2-9.4. Distance and MNREAD acuity were good predictor of the size of BCEA in the better eye only (r^2= 0.42 for visual acuity and r^2= 0.50 for MNREAD acuity), while both acuity measurements were weak predictors of the BCEA in the worse eye (r^2= 0.003 for distance acuity and r^2= 0.07 for MNREAD acuity). The correlations were much weaker for contrast sensitivity for both eyes (r^2= 0.05 for the better eye and r^2= 0.06 for the worse eye). Analysis of covariance was used to investigate whether the slopes of the regression were different for the better and the worse eye for any of the above measurements. There was significant difference between the slopes of the regression lines for the better and the worse eye for distance and MNREAD acuity, but there was no difference for contrast sensitivity (ANCOVA; p=0.04 for distance acuity, p=0.03 for MNREAD acuity, p=0.74 for contrast sensitivity).

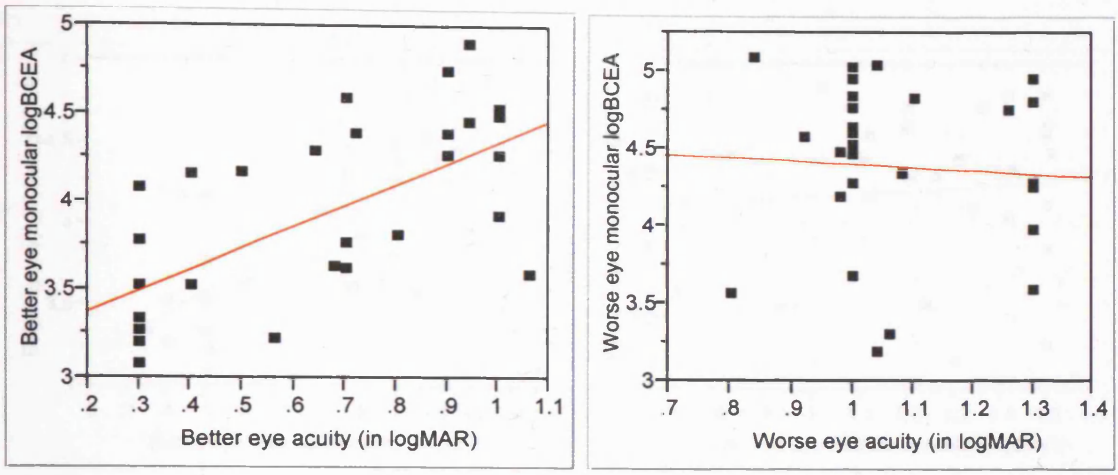


Figure 9.2. Better and worse eye distance visual acuity (in logMAR) against their monocular logBCEAs. The red line represents the best fit linear regression line (r^2= 0.42, p=0.00 for the better eye; r^2= 0.003, p=0.77 for the worse eye).

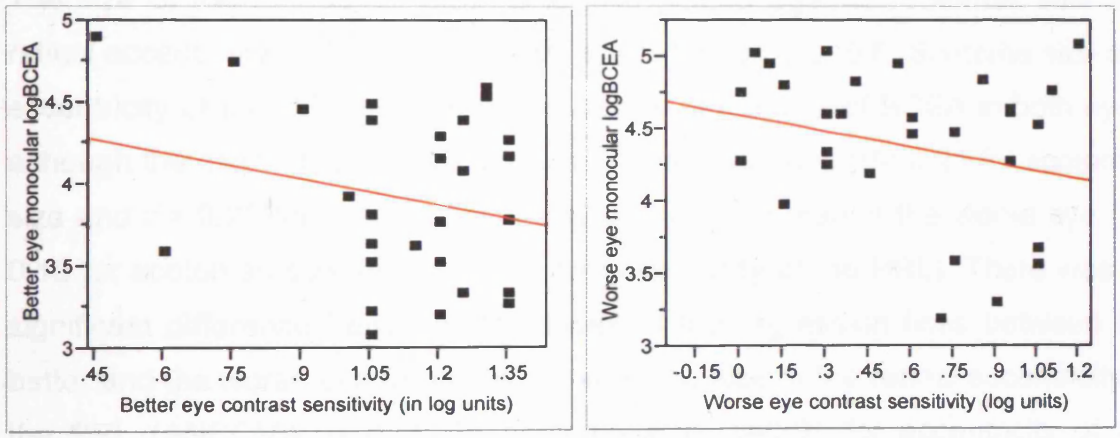


Figure 9.3. Better and worse eye contrast sensitivity (in log units) against their monocular logBCEAs. The red line represents the best fit linear regression line (r^2= 0.05, p=0.23 for the better eye; r^2= 0.06, p=0.17 for the worse eye).

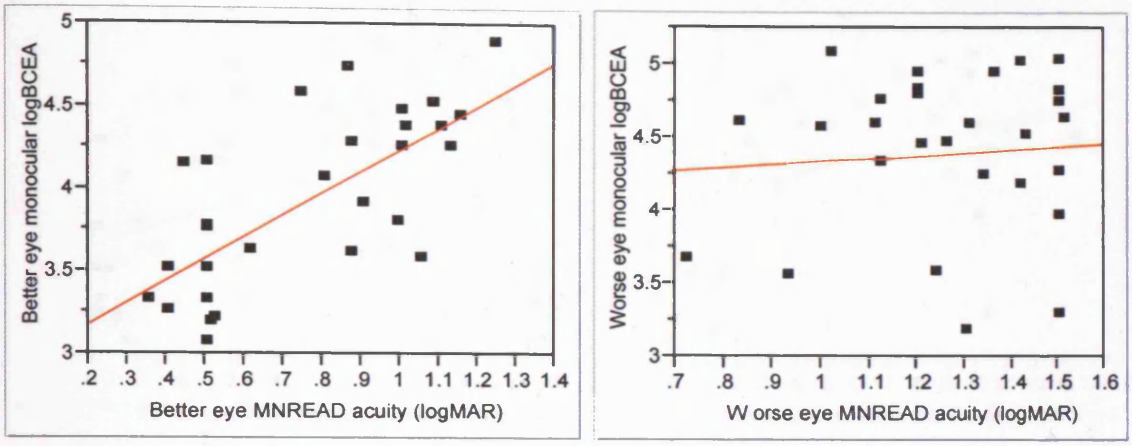


Figure 9.4. Better and worse eye MNREAD acuity (in logMAR) against their monocular logBCEAs. The red line represents the best fit linear regression line (r^2= 0.50, p<0.0001 for the better eye; r^2= 0.007, p=0.65 for the worse eye).

The size of the monocular BCEAs is also plotted against scotomas size and retinal eccentricity of the PRL for each eye in figures 9.5 -9.6. Scotoma size and eccentricity of the PRL were weak predictors of the size of BCEA in both eyes, although the associations were stronger in the better eye (r^2= 0.21 for scotomas size and r^2= 0.25 for retinal eccentricity of the PRL) than in the worse eye (r^2= 0.13 for scotomas size and r^2= 0.09 for eccentricity of the PRL). There was no significant difference between the slopes of the regression lines between the better and the worse eye for either the scotoma size or the retinal eccentricity of the PRL (ANCOVA; p=0.50 for scotoma size; p=0.07 for eccentricity of the PRL).

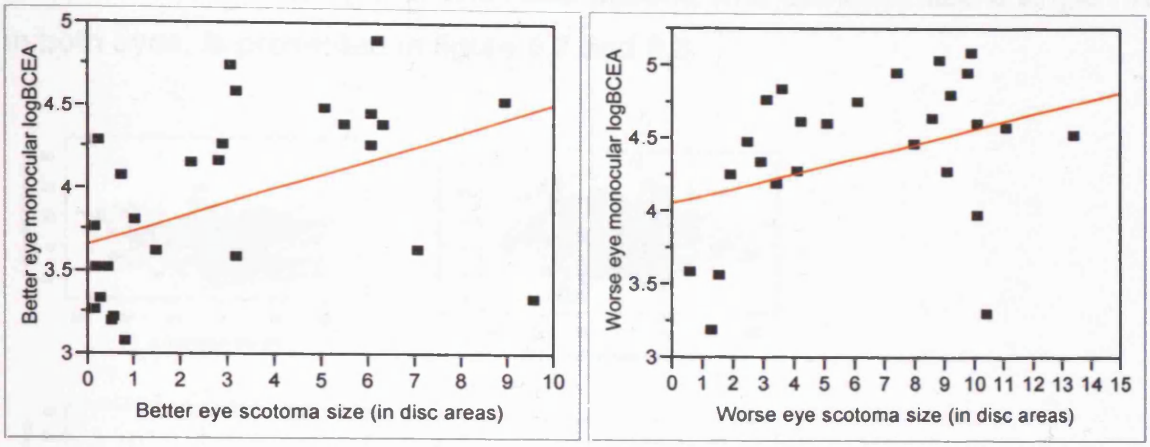


Figure 9.5. Better and worse eye scotoma size (in disc areas) against their monocular logBCEAs. The red line represents the best fit linear regression line (r^2= 0.21, p<0.014 for the better eye; r^2= 0.013, p=0.06 for the worse eye).

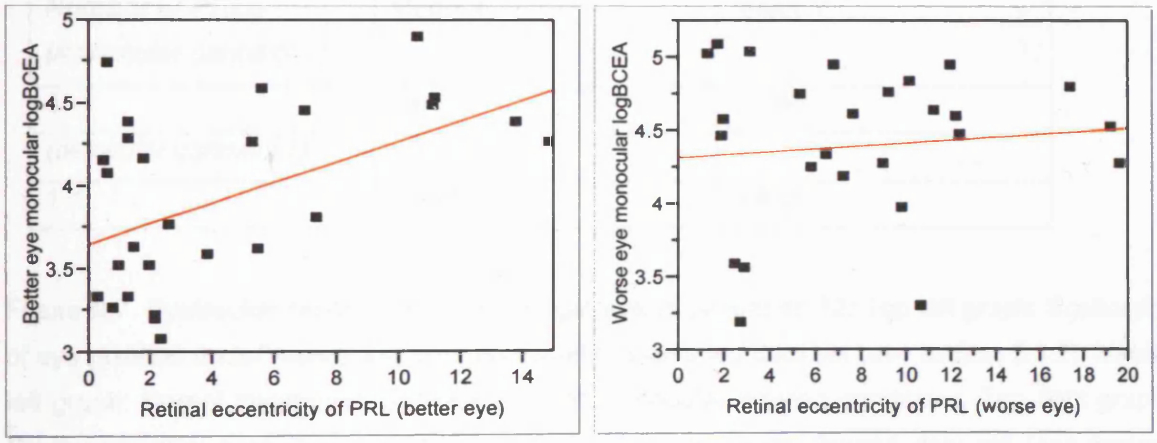
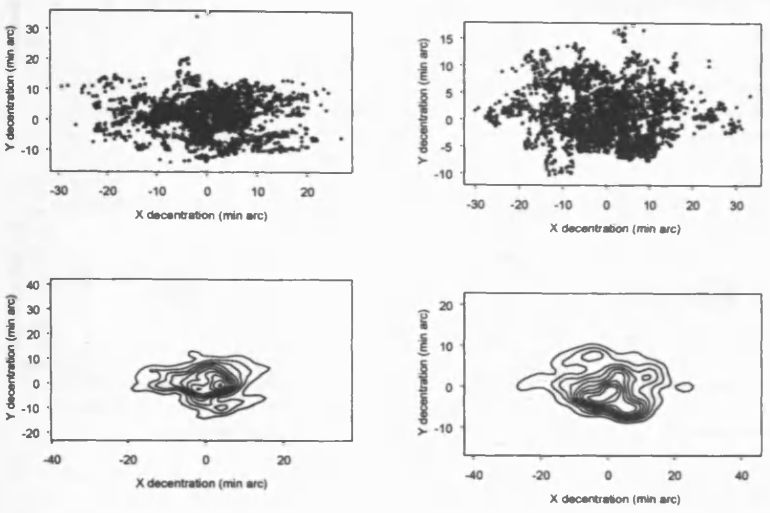


Figure 9.6. Better and worse eye retinal eccentricity of the PRL (in degrees) against their monocular logBCEAs. The red line represents the best fit linear regression line (r^2= 0.25, p=0.006 for the better eye; r^2= 0.09, p=0.62 for the worse eye).

9.2.2. Number of PRLs during monocular viewing conditions and binocular viewing conditions

All AMD patients exhibited only one PRL (example given in figures 9.7 and 9.8) under both viewing conditions for both eyes, except for subject 23, who demonstrated two PRLs in both eyes under both monocular and binocular viewing (figures 9.9 and 9.10).

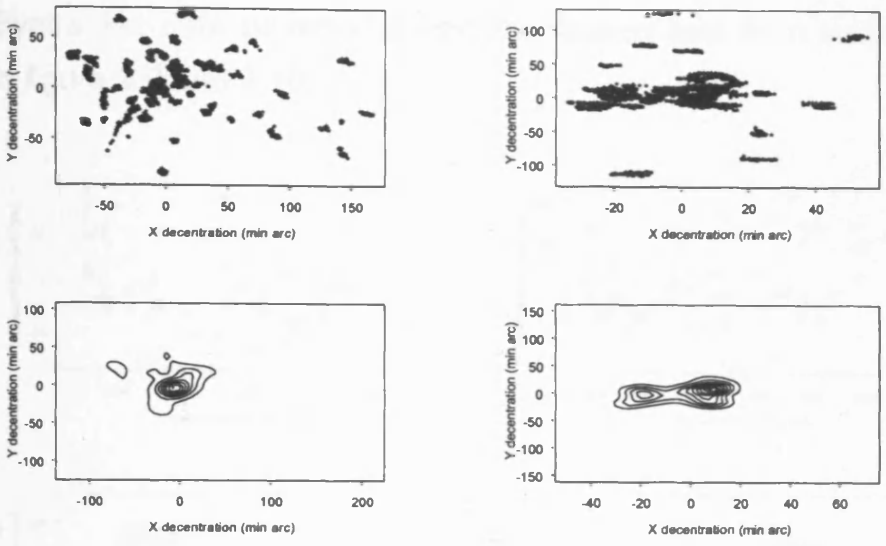
A representative example of one AMD patient, who demonstrated a single PRL in both eyes, is presented in figure 9.7 and 9.8.



Number of PRLs *(monocular conditions)*	***Mean X***	***Mean Y***
1	3.646	-1.956
(binocular conditions)		
1	6.543	3.432

Figure 9.7. Eyetracker recordings from the right eye of patient no 12. Top left graph: Scatterplot of eye position under monocular viewing conditions-cleaned data set (see section 9.1.2), Middle left graph: Kernel distribution of fixation under monocular viewing conditions. Top right graph: Scatterplot of eye position under binocular viewing conditions-cleaned data set (see section 9.1.2), Middle right graph: Kernel distribution of fixation under binocular viewing conditions. Bottom table: mean x and y coordinates of PRL locus in min of arc.

It was evident from the above plots that the patient was using a single PRL in his right eye under both viewing conditions.

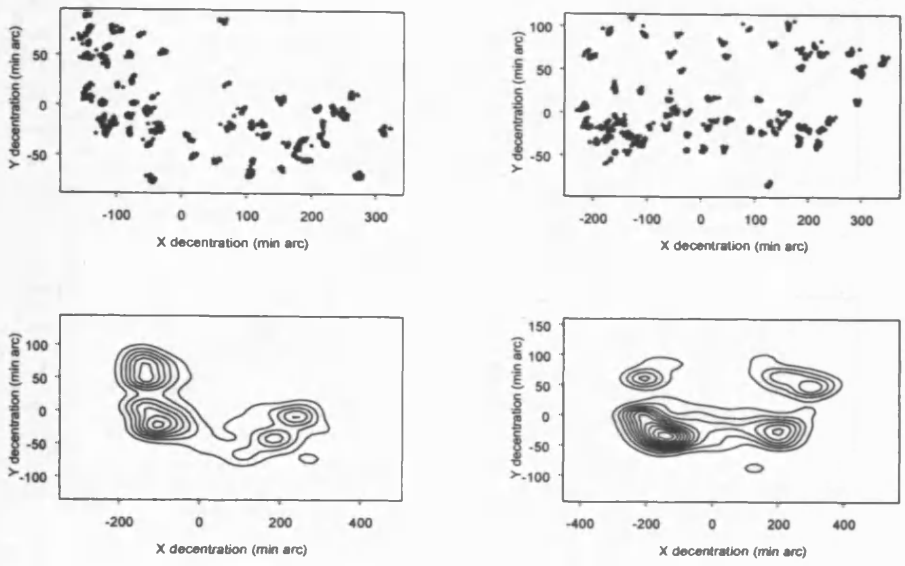


Number of PRLs *(monocular conditions)*	***Mean X***	***Mean Y***	***p***
1	1.342	2.673	
(binocular conditions)			
1	10.432	2.453	0.855
2	-15.735	1.674	0.145

Figure 9.8. SMI recordings from the left eye of patient no 12. Top left graph: Scatterplot of eye position under monocular viewing conditions-cleaned data set (see section 9.1.2), Middle left graph: Kernel distribution of fixation under monocular viewing conditions. Top right graph: Scatterplot of eye position under binocular viewing conditions-cleaned data set (see section 9.1.2), Middle right graph: Kernel distribution of fixation under binocular viewing conditions (note that the scale on the x axis is different from the y axis for top and middle right graphs). Bottom table: mean x and y of PRL locus in min of arc and probability values for the binocular recordings.

The above plot shows that the patient is using 2 different PRLs under binocular viewing conditions. However, the p was <0.20 for the second PRL and the difference in the two loci is less than 3 degrees in the x and y meridian. Therefore, we consider that this patient is using only one PRL (see section 9.1.2.2). We ran the programme again with one PRL and the mean x and y values were: 5.856 and 2.036 respectively and these values were used for subsequent analysis in this study.

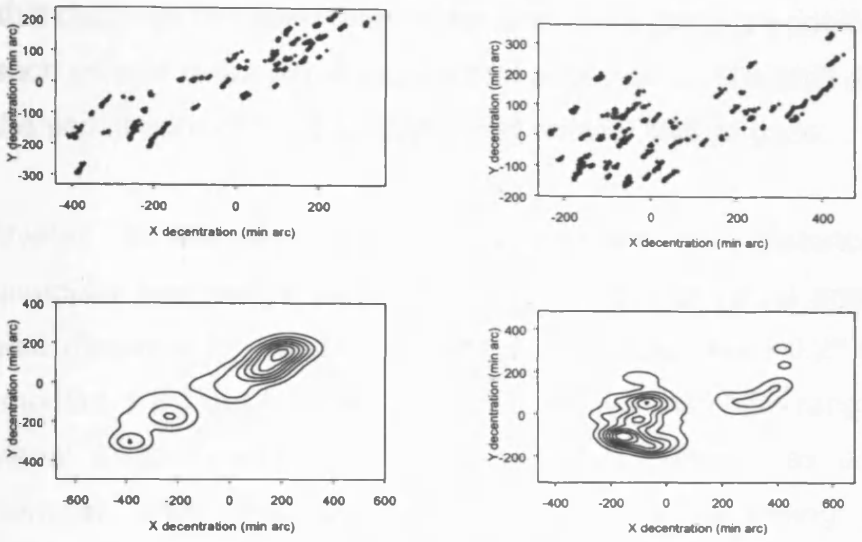
Eyetracker data recorded during the fixation task from subject 23 is presented in figure 9.9 and 9.10.



Number of PRLs *(monocular conditions)*	***Mean X***	***Mean Y***	***p***
1	-105.921	-25.756	0.358
2	240.863	-12.453	0.307
3	167.325	-27.853	0.175
4	-110.856	60.578	0.160
(binocular conditions)			
1	-143.052	-25.094	0.499
2	212.667	-20.978	0.215
3	300.743	49.593	0.160
4	-205.729	60.351	0.126

Figure 9.9. Eyetracker recordings from the right eye of patient no 23. Top left graph: Scatterplot of eye position under monocular viewing conditions-cleaned data set (see section 9.1.2), Middle left graph: Kernel distribution of fixation under monocular viewing conditions. Top right graph: Scatterplot of eye position under binocular viewing conditions-cleaned data set (see section 9.1.2), Middle right graph: Kernel distribution of fixation under binocular viewing conditions. Bottom table: mean x and y of multiple PRL loci in min of arc and probability values.

From the above plot, only two PRLs were taken into account as for the third and fourth PRLs under both monocular and binocular conditions p were <0.20 (see section 9.1.2.2).



Number of PRLs *(monocular conditions)*	***Mean X***	***Mean Y***	***p***
1	109.644	96.475	0.655
2	-217.353	-203.479	0.345
(binocular conditions)			
1	-94.900	-37.283	0.766
2	309.881	101.741	0.234

Figure 9.10 SMI recordings from the left eye of patients 23. Top left graph: Scatterplot of eye position under monocular viewing conditions-cleaned data set (see section 9.1.2), Middle left graph: Kernel distribution of fixation under monocular viewing conditions. Top right graph: Scatterplot of eye position under binocular viewing conditions-cleaned data set (see section 9.1.2), Middle right graph: Kernel distribution of fixation under binocular viewing conditions. Bottom table: mean x and y of multiple PRL loci in min of arc and probability values.

In the above example both PRLs were taken into account as p were >0.20 for both viewing conditions and they differ by more than 3 degrees under both viewing conditions.

9.2.3. Changes in gaze position during monocular versus binocular recordings

The shift of gaze position from monocular to binocular viewing conditions for each eye for twenty nine AMD subjects (subject 23 was excluded since he demonstrated multiple PRLs) was calculated in degrees of visual angle and the shift distance between monocular and binocular gaze positions for both eyes for each patient is shown in table 9.b in appendix 2. The shift distance is defined as the vector sum of the horizontal and vertical shift of gaze.

Overall, in the AMD group the calculated shift distance from monocular to binocular recordings varied from 0.2° to 22° of visual angle (median 2.5°). The shift distance for the better seeing eye varied from 0.2° to 12° of visual angle (median 1.2°) but for the worse seeing eye the shifts ranged from 0.5° to 22° of visual angle (median 5.6°) (Figure 9.11). There was a significant difference between shift distances in better- and worse-seeing eyes (Wilcoxon test, $p<0.0001$), with smaller distances recorded in the better eye.

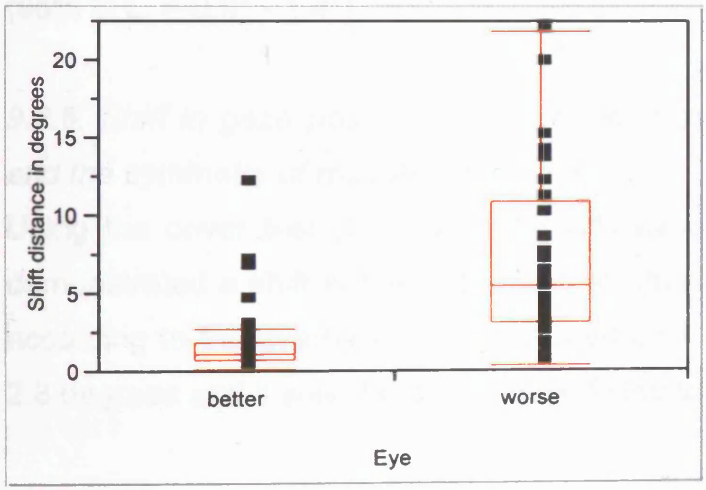


Figure 9.11. The distribution of the shift distance (in degrees of visual angle) is plotted for the better and the worse eye for the AMD patients. Each distribution is summarized by a quantile box plot showing the 90th, 75th, 50th (median), 25th and 10th percentiles.

9.2.4. Normal data and definition of 'shift' in gaze position

In the normal group the calculated shift distance from monocular to binocular recordings varied from 0.3° to 2.2° of visual angle (mean 1.1° ± 0.6° SD). In order to decide when the value of the shift distance demonstrated a different retinal locus used for fixation, we accepted as a cut off point the value of 2.3°

(mean + 2 SD of the normal subjects) as our main concern was to avoid considering a normal shift as abnormal (type I error).

According to that criterion, five AMD patients showed no change in gaze position in either eye. Five patients demonstrated a shift in both eyes, while the remaining nineteen patients demonstrated a shift only in one eye. Wherever there was a shift in only one eye the shift was observed in the worse eye. Furthermore, the worse eye determined the biggest shift whenever there was a shift in both eyes except for case 1. Patient no 1 had equal distance acuities and the worse eye was determined based on contrast sensitivity measurements.

9.2.5. Repeatability of binocular recordings

For the normal group the mean of the difference in the shift distance between the first and second recording was 0.3° (95% C.L.= 0.0° - 0.7°). For the AMD group the mean of the difference between the two measurements was 0.2° (95% C.L. =-0.9° - 1.4°).

9.2.6. Shift in gaze position and its relation to the cover test, ability for fusion and the symmetry of macular scotomas

Using the cover test (5.3.1 and 7.2.2.1) we detected all but one patient that demonstrated a shift in their gaze position from monocular to binocular viewing according to the eyetracker results. In subject 18 the shift in gaze position was 2.8 degrees and it was the one that we failed to detect it clinically.

By combining data from the test assessing binocular fusion (using the CrystalEyes glasses system- section 5.3.3 and 7.2.2.3) and eyetracker data we concluded that all patients that exhibit no shift in their PRL in either eye from monocular to binocular viewing showed evidence of local fusion. Of the patients that showed a shift in both eyes only one patient (20%) perceived the cross. Of the patients that demonstrated a shift only in their worse eye only 3 patients (15.7%) elicited fusion (Figure 9.12). There was a significant difference between patients that demonstrated ability for fusion at the PRL with respect to the shift in gaze position (Chi-square, p=0.0012).

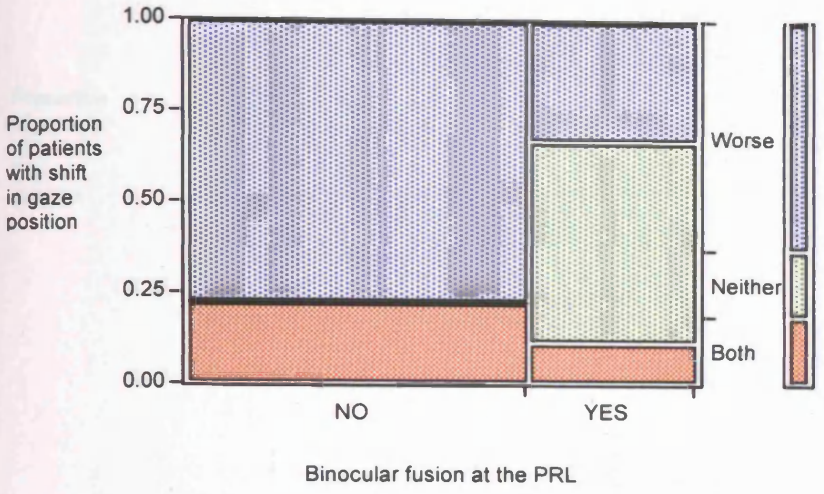


Figure 9.12. Proportion of patients who showed a shift in gaze position (both eyes, neither eyes, worse eye) from monocular to binocular recording conditions is plotted for two groups (patients with evidence and absence of fusion at the PRL). YES= evidence of fusion, NO= absence of fusion. The width of the columns represents the proportions of patients with evidence and absence of fusion. In particular, there was evidence of fusion in 31% of patients, while the rest showed no fusion.

Four of nine patients (44.4%) with symmetrical scotomas showed no shift in gaze position while three patients (33.3%) showed a shift only in the worse eye under binocular viewing. Two patients (22.2%) showed a shift in both eyes (figure 9.13). From the eighteen patients with asymmetrical scotomas 77.7 % showed a shift in their worse eye while three patients (16.6%) showed a shift in both eyes. One patient (5.5 %) showed no shift in either eye; this patient used a central island of vision to fixate in their worse eye (subject no 28). There was a significant difference between patients with symmetrical and asymmetrical scotomas with respect to the shift in gaze position (Chi-square, p=0.03).

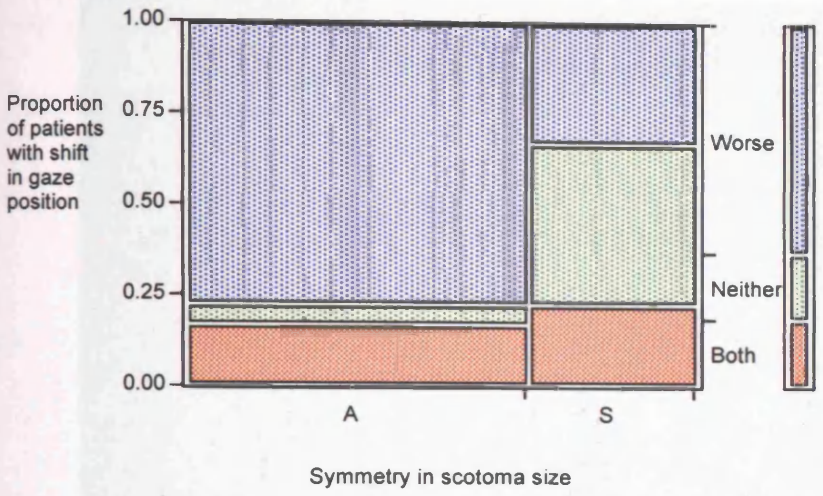


Figure 9.13. Proportion of patients who showed a shift in gaze position (both eyes, neither eyes, worse eye) from monocular to binocular recording conditions is plotted for two groups (patients with symmetrical and asymmetrical scotomas). S= symmetrical scotomas, A= asymmetrical scotomas. The width of the columns represents the proportions of patients with symmetrical and asymmetrical scotomas. In particular, 66.6% of patients had asymmetrical scotomas, while the rest had symmetrical scotomas.

9.2.6. Binocular fixation locus

9.2.6.1. Retinal location of binocular PRLs

We assumed that patients were using the same PRL to fixate the target under monocular viewing conditions during recording on the SLO and the eyetracker. Thus, the shift of position of gaze recorded by the eyetracker from monocular to binocular viewing conditions could be superimposed on the monocular PRL on the SLO image and the resultant retinal locus was defined as the binocular PRL (figure 9.14).

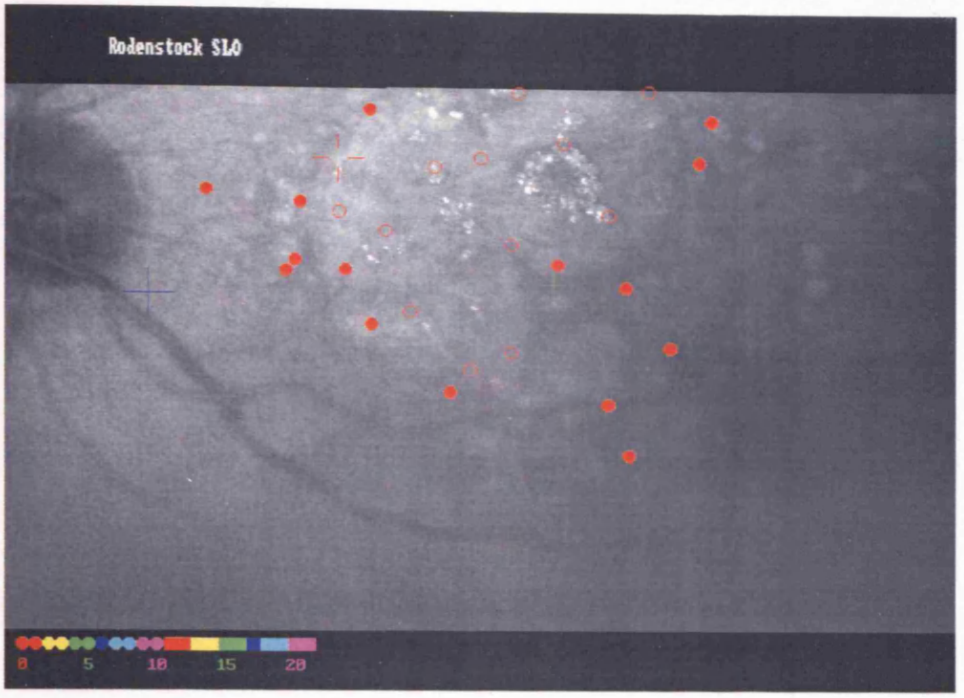


Figure 9.14. SLO infrared images of the left fundus of one AMD patients with microperimetry maps of the scotomatous areas. The red cross represents the monocular retinal locus used for fixation of the target during SLO recordings. The blue cross indicates the centre of the area that was used as a landmark to compensate for eye movements. The green cross represents the calculated retinal locus used for fixation under binocular viewing conditions.

The binocular PRLs fell outside the absolute macular scotomas in both eyes in 20 AMD patients while in the remaining 7 patients they fell within the absolute macular scotomas in the worse eye. As was expected, none of latter 7 patients showed binocular fusion. Nine of the twenty patients (45%), whose binocular fixation loci fell on 'seeing areas', showed evidence of fusion, while the rest failed to perceive the cross (section 5.3.2 and 7.2.2.3).

9.2.6.1. Distance of binocular fixation locus from 'fovea'

The distance between the binocular fixation locus and the fovea (DBFF) was calculated for both eyes for all tested subjects in degrees of visual angle based on the SLO images in a similar way to that in section 8.2.3. All data were calculated in pixels and were converted to degrees of visual angle and are presented in detail in table 9c, in appendix 2. Figure 9.15 presents the DBFF for both eyes for all tested AMD subjects. There was no significant difference in the distance from binocular fixation to fovea between the better and the worse eye (unpaired t-test, p=0.58).

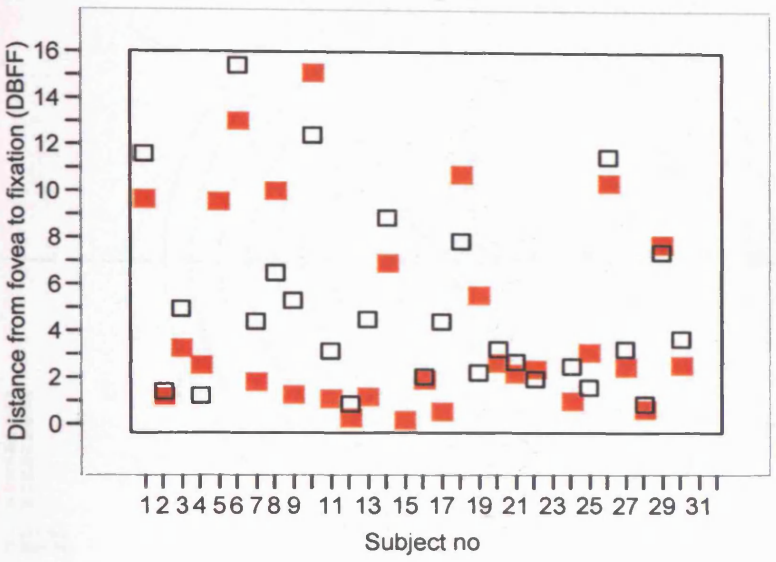


Figure 9.15. Distances from fovea to binocular fixation locus (DBFF) are presented for both eyes for each AMD subject. Red squares represent the better eye and black squares represent the worse eye. Subjects no 5 and 15 have only data from their better eye. Subject 23 has no data from either eye as he has been excluded from subsequent data analysis (multiple PRLs in both eyes).

9.2.6.2. Assessment of retinal correspondence of binocular PRLs

Figure 9.16 maps the actual location of the binocular PRLs on the retina with respect to the fovea separately for patients with symmetrical and asymmetrical scotomas. The location of the PRLs has been calculated in degrees of visual angle.

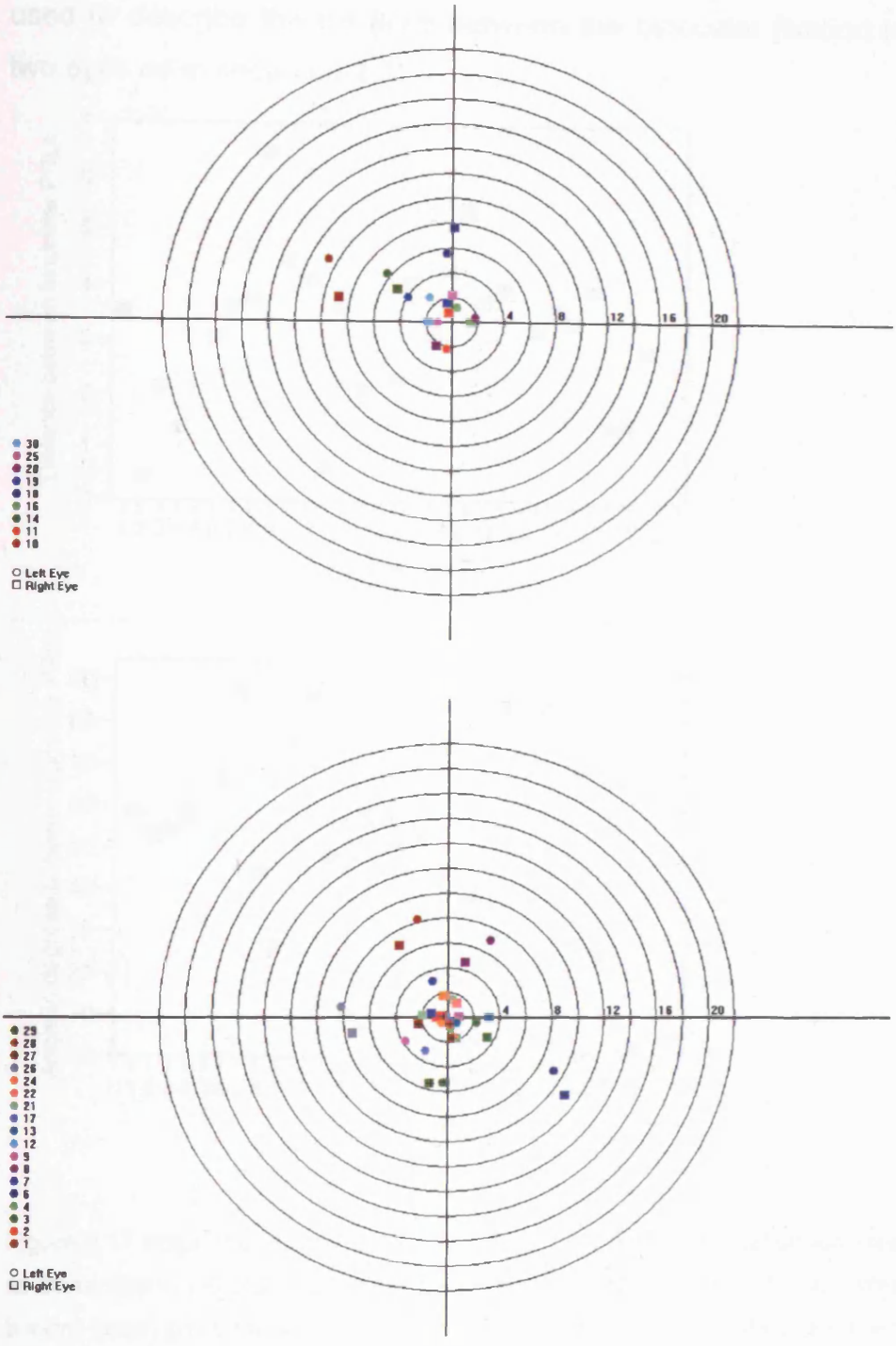


Figure 9.16 maps the actual location of the binocular PRLs on the retina with respect to the fovea separately for patients with symmetrical and asymmetrical scotomas. The location of the PRLs has been calculated in degrees of visual angle.

In order to evaluate the retinal correspondence between the two binocular PRLs we calculated the distance between the two fixation loci. Polar coordinates were

used to describe the distance between the binocular fixation loci used by the two eyes as in section 8.2.6.

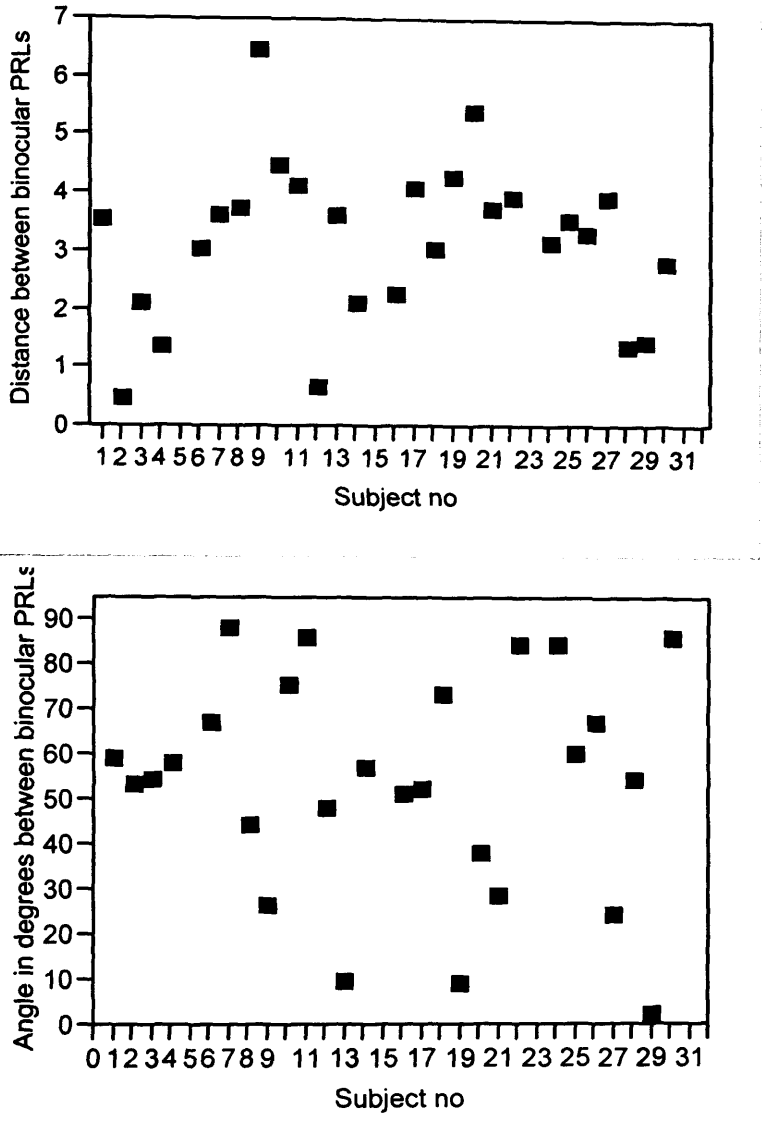


Figure 9.17 maps the relative distance between the binocular fixation loci used by the two eyes as in section 8.2.6.The top graph plots the magnitude of the distance between them and the bottom graph plots the angle between the two loci. Detailed data are presented in table 9c in appendix 2.

The magnitude of these distances ranged from 0.4° to 6.4° (mean 3.1° ±1.3° SD) and the angle between the binocular loci varied from 1.7° to 87.9° (mean 53.2° ±24.6° SD). The distance between the binocular PRLs position and the angle between them was measured separately for AMD patients with symmetrical and asymmetrical scotomas. In patients with symmetrical scotomas the mean distance between the two loci was 3.5° ± 1.1°SD, while in patients with asymmetrical scotomas the mean distance was 2.9° ± 1.4° SD. There was

no statistical difference between the two groups (unpaired t-test, p-value=0.29). With respect to the angle between the binocular PRLs between the two eyes patients with symmetrical scotomas demonstrated a mean of 59.5° ± 24.8° SD and patients with asymmetrical scotomas had a mean of 50° ± 24.6° SD. No significant difference was found between them (unpaired t-test, p=0.36).

When the distances between the two monocular PRLs were compared to the distances between the two binocular PRLs in patients with symmetrical scotomas we found no significant difference between them (paired t-test, p=0.85). However, in patients with asymmetrical scotomas there was a significant difference in the distances between the monocular and binocular PRLs (paired t-test, p<0.0001) (figure 9.18).

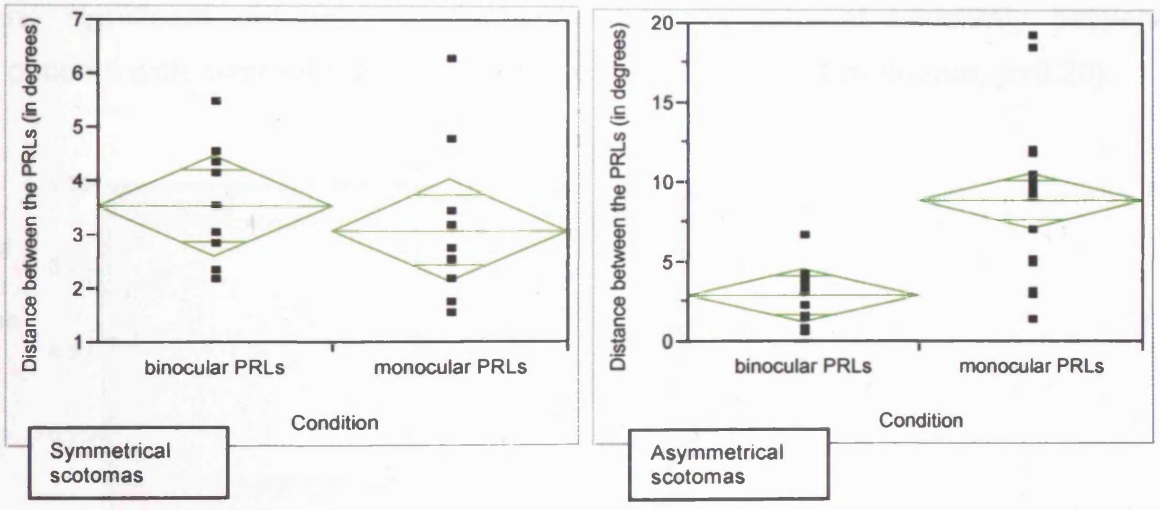


Figure 9.18. Distance (in degrees of visual angle) between the monocular and the binocular PRLs in patients with symmetrical scotomas (left figure) and asymmetrical scotomas (right figure). The line across each diamond represents the group mean. The vertical span of each diamond represents the 95% confidence interval for each group.

In order to evaluate the retinal correspondence between the two binocular PRLs we measured the distance between the two fixation loci separately for the horizontal and the vertical meridian. The range of these distances was 0.1° - 5.7° (mean 1.7° ±1.4° SD) in the horizontal meridian and 0.0°4 - 4.3° in the vertical meridian (mean 2.2° ±1.2° SD). Table 9.d in appendix 2 presents these distances separately for patients with symmetrical and asymmetrical scotomas. There was no significant difference in the distance in the horizontal or in the vertical meridian between patients with symmetrical and asymmetrical

scotomas (unpaired t-test, p=0.98 for the horizontal meridian and p=0.18 for the vertical meridian).

9.2.7. Binocular performance in clinical tests and its relationship with the interocular symmetry of macular scotomas

There was no binocular gain in distance acuity (figure 7.2 and 7.5). We looked at binocular gain for contrast sensitivity and MNREAD acuity in patients with symmetrical and asymmetrical scotomas. 3 patients (33.3%) with symmetrical scotomas had positive gain and 6 patients (66.6%) had no binocular gain for contrast sensitivity. Nobody exhibited evidence of negative gain. 14 patients with asymmetrical scotomas (77.7%) had no binocular gain, two patients (11.1%) had positive gain and two had negative gain (Figure 9.19). There was no significant difference in binocular gain in contrast sensitivity between patients with symmetrical and asymmetrical scotomas (Chi-square, p=0.20).

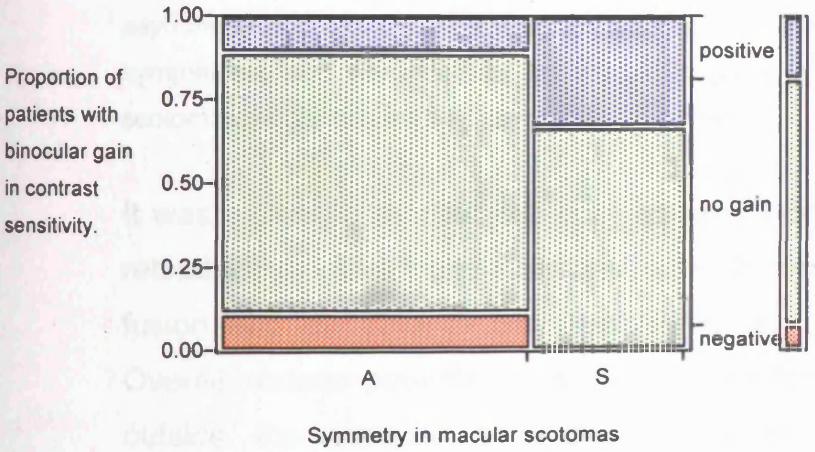


Figure 9.19. Proportion of patients who showed a binocular gain in contrast sensitivity (positive gain, negative gain, no gain/ within test-retest variability of the test) is plotted for two groups (patients with symmetrical and asymmetrical scotomas). S= symmetrical scotomas, A= asymmetrical scotomas. The width of the columns represents the proportions of patients with symmetrical and asymmetrical scotomas. In particular, 66.6% of patients had asymmetrical scotomas, while the rest had symmetrical scotomas.

7 patients (77.7%) with symmetrical scotomas had neither positive nor negative binocular gain in MNREAD acuity. One patient (11.1%) exhibited positive gain and another one negative gain. 13 patients with asymmetrical scotomas (72.2%) had no binocular gain, 4 patients (22.2%) had positive gain and one

patient (5.5%) had negative gain (Figure 9.20). There was no significant difference in binocular gain in MNREAD acuity between patients with symmetrical and asymmetrical scotomas (Chi-square, p=0.70).

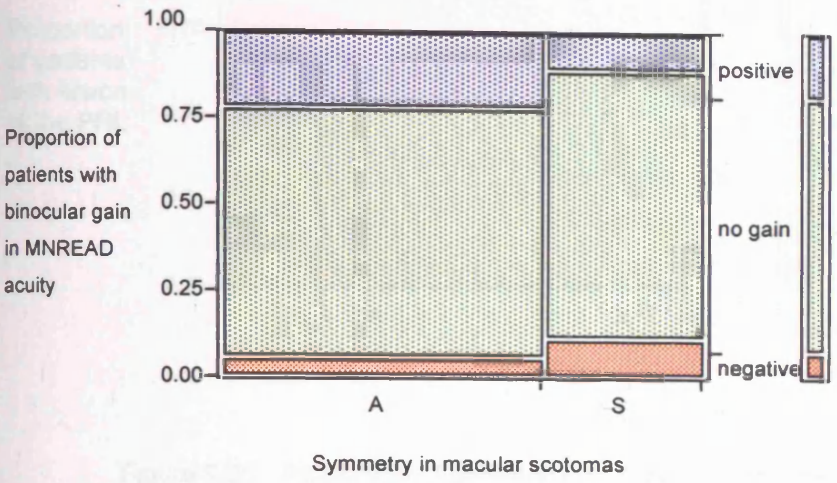


Figure 9.20. Proportion of patients who showed a binocular gain in MNREAD acuity (positive gain, negative gain, no gain and/or within test-retest variability of the test) is plotted for two groups (patients with symmetrical and asymmetrical scotomas). S= symmetrical scotomas, A= asymmetrical scotomas. The width of the columns represents the proportions of patients with symmetrical and asymmetrical scotomas. In particular, 66.6% of patients had symmetrical scotomas, while the rest had asymmetrical scotomas.

It was expected that all subjects whose binocular PRLs fell on corresponding retinal locations in both eyes and outside the scotomatous areas would retain fusion and be able to perceive the cross (see section 5.3.3 and 7.2.2.3). Overall, sixteen patients showed binocular corresponding retinal points that fell outside the macular scotomas. However, only 8 patients reported the perception of a cross during the task. Interestingly, one patient (subject 11) perceived the cross although his binocular PRLs were considered to fall on non corresponding retinal areas. As was expected, none of the patients whose PRLs fell within the scotomas in the worse eye were able to perceive the cross.

With respect to fusion at the binocular fixation loci (see section 5.3.2 and 7.2.2.3) the majority of patients (66.6%- 6 of 9 patients) with symmetrical scotomas demonstrated fusion. In contrast, for patients with asymmetrical scotomas only 16.6% (3 of 18 patients) showed evidence of fusion and perceived the cross (Figure 9.21). There was a significant difference in ability for fusion at the PRL between patients with symmetrical and asymmetrical

scotomas (Chi-square, p=0.009).

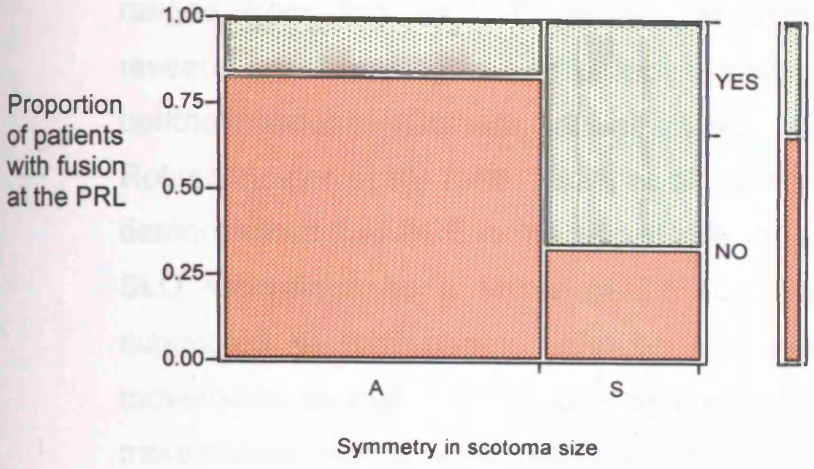


Figure 9.21. Proportion of patients who showed fusion near the PRL (YES= evidence of fusion, NO= absence of fusion) is plotted for two groups (patients with symmetrical and asymmetrical scotomas). S= symmetrical scotomas, A= asymmetrical scotomas. The width of the columns represents the proportions of patients with symmetrical and asymmetrical scotomas. In particular, 66.6% of patients had symmetrical scotomas, while the rest had asymmetrical scotomas.

All nine patients with symmetrical scotomas showed binocular PRLs that fell outside the scotomas and 7 of them demonstrated corresponding binocular PRLs. However, only five of the seven patients (71.4%) perceived the cross.

Of the 18 patients with asymmetrical scotomas, 7 had PRLs that fell within the scotomas in one eye and 2 demonstrated non corresponding binocular PRLs. The remaining 9 patients were to fuse the target. However, only 3 patients of them (33.3%) showed evidence of fusion.

9.3. Discussion

9.3.1. Fixation stability during monocular and binocular recordings

On average, fixation stability is impaired in AMD patients but there is large inter-subject variability in BCEA size. Previous reports of BCEAs in AMD patients vary from near normal values (80-370 min of arc²) (Steinmann 1965; Kosnik et al. 1986; Culham et al. 1993) to over 13,000 min of arc² (Culham et al. 1993;

Schuchard and Fletcher 1994; Schuchard et al. 1994; Rohrschneider et al. 1995). Our patients demonstrated much larger values than these (our BCEAs ranged from 851 to 217,966 min of arc^2). However, most of the prior researchers investigated fixation stability using the scanning laser ophthalmoscope (Culham et al. 1993; Schuchard and Fletcher 1994; Rohrschneider et al. 1995; Tezel et al. 1996; Nilsson et al. 1998). It has been demonstrated that BCEAs measured with the eyetracker are larger compared to SLO recordings by a factor of 2.5 (Crossland and Rubin 2002). As was suggested in that paper, although the eyetracker compensates for head movements so that the true gaze position rather than eye position is recorded, more retinal motion could result in greater BCEAs when using the eyetracker. There are only a few reports on fixation stability using an eyetracker (Kosnik et al. 1986; Crossland and Rubin 2002; Bellmann et al. 2004; Crossland et al. 2004b).

In addition, most of the investigators have included recordings from the better eye only (the worse eye was excluded from the studies) and consequently smaller BCEAs have been obtained. The BCEAs from the better eye of our patients under monocular viewing conditions (median: 7943 min of arc^2, mean: 15514 min of arc^2, range: 1120-74346 min of arc^2) were still higher than the mean values of 7480 min of arc^2 reported by Crossland et al (Crossland and Rubin 2002; Crossland et al. 2004b), who tested patients with newly acquired macular disease, but they are more consistent with the mean values of BCEAs reported by Bellmann et al (their mean values ranging from 12052 min of arc^2 ± 254% to 23109 min of arc^2 ± 298% depending on the fixation target used (Bellmann et al. 2004).

There was no significant difference in fixation stability when patients were using the better eye or both eyes to fixate the target ($p=0.65$). However, fixation stability improved significantly ($p>0.05$) in the worse eye when the subject was viewing binocularly compared to monocular viewing. There was a good correlation between the binocular BCEA in both eyes ($r=0.76$). These results indicated that binocular fixation stability is mainly driven by the 'better' eye.

We found that distance and MNREAD acuity were good predictors of the size of BCEAs only in the better eye (r^2=0.42 for distance acuity and r^2=0.50 for MNREAD acuity). On the other hand, distance and MNREAD acuity in the worse eye and contrast sensitivity in both eyes were poor predictors of the BCEA. The difference in the associations between the better and the worse eye were significant different for both measurements (distance and MNREAD acuity). Crossland et al. showed poor correlations between the size of BCEA and both distance acuity and contrast sensitivity (r=0.33 for distance acuity and r= 0.00 for contrast sensitivity) although he tested the better eye, but he examined a different group of patients than ours: patients with newly acquired macular disease both AMD and juvenile cases (Crossland et al. 2004b).

Although it has been reported that as retinal eccentricity increases, fixation stability becomes more compromised (Sansbury et al. 1973), we found that both scotoma size and retinal eccentricity of the monocular PRL were weak predictors of the size of BCEA, which was in accordance with previous reported results by Timberlake et al, White and Bedell and Crossland et al (Timberlake et al. 1986; White and Bedell 1990; Crossland et al. 2004c). However, we found stronger associations for the better eye (r^2=0.21 for scotoma size and r^2=0.25 for eccentricity of the PRL) compared with the worse eye, although there was no significant difference in the associations between the better and the worse eye neither for scotoma size or retinal eccentricity of the PRL.

9.3.2. Number of PRLs during monocular viewing conditions and binocular viewing conditions

During this study we found only one patient out of thirty (3.3%) was using multiple PRLs in both eyes under both viewing conditions. Previous researchers have reported higher percentages of AMD patients exhibiting multiple PRLs. Crossland et al and Whittaker et al. reported percentages as high as 44%. However, these groups have investigated patients with newly acquired macular disease and visual loss (Crossland et al. 2004c), the task was more complicated (Whittaker et al. 1988; Deruaz et al. 2002), or the subjects were using multiple PRLs under different lighting conditions (Lei and Schuchard 1997).

9.3.3. Changes in gaze position during monocular versus binocular recordings

When we compared binocular viewing behaviour to monocular in subjects with bilateral AMD during a fixation task, 82.7% of them (24 patients) demonstrated a shift in their gaze position either in one eye or both eyes, when they changed from monocular to binocular viewing. The measured shifts exceeded the shifts observed in normally-sighted patients (≤ 2.3°) and cannot be attributed to test-retest variability observed for AMD patients (~2.3°). As there was a significant difference between the shift distance in the better and the worse eye with the smaller shift recorded in the better eye, we concluded that the better eye kept the gaze position or changed less than the worse eye when switching from monocular to binocular viewing of the target (figure 9.11).

As far as we are aware there are only very limited reports of binocular fixation and function in AMD patients (Schuchard and Fletcher 1994; Schuchard et al. 1995; Schuchard et al. 2003). Schuchard et al.(Schuchard and Fletcher 1994; Schuchard et al. 1995) first reported that some AMD subjects may use monocular PRLs that fall on non corresponding retinal areas. By using an SLO for monocular recordings combined with a psychophysical task to test the effect of this incongruity they concluded that binocular fixation tasks were driven by the 'dominant' eye. More recently, the same group attempted to produce binocular SLO results by combining monocular SLO data but, as they indicated, the main limitation was the inability to accurately predict gaze position in binocular viewing (Schuchard et al. 2003). In that respect, our study is the first to document the changes in gaze position under binocular versus monocular viewing in AMD patients.

9.3.4. Shift in gaze position and its relation to the cover test, ability for fusion and the symmetry of macular scotomas

We detected clinically using the cover test all the patients, except from one that demonstrated a shift in their gaze position from monocular to binocular viewing. Although the cover test is a quick and useful clinical procedure for assessing gaze position, its accuracy depends on the examiner's experience. It has been claimed that shifts as small as 1.0^{Δ} or even 0.5^{Δ} can be detected by experienced clinicians (von Noorden and Campos 2002). However, it is generally accepted that 3^{Δ} to 4^{Δ} change (equivalent to 1.7° of arc to 2.3° of arc)

in eye position is required for reliable detection (Romano and von Noorden 1971; von Noorden and Campos 2002). Occasionally, an overshoot of the eye assuming fixation can be observed with a secondary corrective eye movement (rebound saccade) (Mehdorn and Kommerell 1978). In that case examination requires more experience for accuracy. In our study we failed to detect one case that demonstrated a shift in his gaze position, which was, however, very close to the normal values (shift in his gaze position: 2.8° with accepted normal values of 2.3°). Therefore, the eyetracker can be used as an alternative for more objective and accurate documentation of changes in gaze position, which is needed for further evaluation of binocular behaviour in these patients.

AMD patients that were using the same PRLs to fixate under monocular versus binocular viewing conditions (exhibiting no shift in their PRL in neither eye) demonstrated fusion near their PRLs. Only the minority of patients, who showed a shift either in one or both eyes, retained fusion at the fixation loci indicating either the fact that fixation loci fell within the scotomas in the worse eye or retinal correspondence was disrupted and fusion was inhibited.

44.4% of patients with symmetrical scotomas (4 of 9 patients) showed no shift in gaze position when switching from monocular to binocular viewing, while the majority of patients with asymmetrical scotomas (77.7 %) showed a shift in their worse eye. Furthermore, there was significant difference between patients with symmetrical and asymmetrical scotomas with respect to the shift in gaze position. Therefore, our data partially support hypothesis 2 which states that in patients with symmetrical scotomas no shift in gaze position is expected from monocular to binocular viewing and they are expected to use the same PRLs under both viewing conditions in both eyes. However, patients with asymmetrical scotomas are expected to use different PRLs under binocular versus monocular viewing in the worse eye.

9.3.4. Assessment of retinal correspondence of binocular PRLs

According to hypothesis 3 'the binocular PRLs will have similar retinal eccentricities between the two eyes and they will fall on corresponding retinal areas; no difference is expected in patients with symmetrical versus

asymmetrical scotomas'. Our data partially support this hypothesis as will be explained below.

There was no significant difference in the distance from binocular fixation to fovea between the two eyes for all patients (p=0.58), which is in accordance with the above hypothesis.

We followed the same definition for retinal correspondence as in chapter 8 (section 8.3.4). Therefore, we considered as corresponding retinal points those which, when simultaneously stimulated, give rise to the percept of a single object (Millidot, Dictionary of Optometry).

As in chapter 8 (section 8.3.4), we calculated the distances between the two binocular PRLs separately in the horizontal and the vertical meridians. The range of the distance between the binocular PRLs was 0.1° -5.7° (mean 1.7° ±1.4° SD) in the horizontal meridian and 0.0°4 - 4.3° (mean 2.2° ±1.2° SD) in the vertical meridian. As most of these distances fell outside Panum's area we calculated the measurement errors that could account for some of these results. We listed the possible sources of measurement error in table 9.2 below.

Table 9.2 Sources of measurement errors during calculation of distances between binocular PRLs (horizontal and vertical meridian).

Source of measurement errors		
Prediction of centre of blind spot on SLO images (section 6.2.2)	Width of 95% CL	0.5° horizontally 0.6° vertically
Distance of the fovea to the centre of the blind spot (table 6.2)	Width of 95% CL	2.4° horizontally 0.8 vertically
Calculation of shift in gaze position from monocular to binocular viewing using the eyetracker (section 9.2.5)	Width of 95% CL	1.5° horizontally 2.3° vertically

In order to compare our results with this table the distances between the two PRLs separately in the horizontal and the vertical meridian were taken into account as in chapter 8. We looked at these differences for the patients with symmetrical scotomas (see table 9.d, appendix 2) and we compared them with the total measurement error distances from the above table (overall, horizontally: 4.4° and vertically: 3.7°). All patients demonstrated distances that fell within the measurement error areas in the horizontal meridian and seven patients (subject no 14, 16, 18, 19, 20, 25 and 30) in the vertical meridian. If we take into consideration both meridians the distances between the two binocular PRLs could be attributed to measurement errors in seven of nine patients (77.7%) (subject no 14, 16, 18, 19, 20, 25 and 30). From the patients with asymmetrical scotomas all but one patient (except subject no 9) demonstrated distances that fell within the measurement error areas in the horizontal meridian and all but one patient (except subject no 22) in the vertical meridian. When both meridians were taken into account, sixteen of eighteen patients (88.8%) showed distances between the two binocular PRLs that could be explained from measurement errors.

The distances between the two binocular PRLs that exceeded the amount that could be explained by Panum's area and measurement error area were 1.3 degrees horizontally and mean 0.3 degrees (range 0.1 – 0.6) vertically. Although the above measurements are small we considered that these patients (subject no 9, 10, 11 and 22) could be using non corresponding retinal areas when viewing binocularly. This suggests that there may have been strabismus in some patients but we have no independent evidence of heterotropia.

We found no difference in the distance between the binocular PRLs between patients with symmetrical and asymmetrical scotomas ($p=0.29$ for the overall magnitude of the distance between the two PRLs; $p=0.98$ for the difference in the distance between the PRLs in the horizontal meridian; $p=0.18$ for the difference in the distance between the two PRLs in the vertical meridian), which was in accordance with hypothesis 3.

However, there was a significant difference in the distances between the two monocular PRLs compared to the distances between the two binocular PRLs in

patients with asymmetrical scotomas ($p<0.0001$), but not in patients with symmetrical scotomas ($p=0.85$), indicating that binocular PRLs tend to fall on more corresponding retinal areas than monocular PRLs in patients with asymmetric scotomas.

Schuchard et al (Schuchard et al. 1995) reported a lower percentage of retinal correspondence in both meridians compared to our results. Specifically, they concluded that only 40% of their patients had retinal correspondence of their binocular PRL in both the horizontal and vertical directions, 10% only vertically, none horizontally and 50% in neither direction. However, retinal correspondence was based on the location of the monocular PRLs as identified using an SLO and the assumption of patients using the same monocular and binocular PRLs was made. Although, the correspondence was based on the interocular distance in retinal distances between the physiological blind spot and the PRL, it was not mentioned in their paper how they determined retinal correspondence of the PRLs.

9.3.5. Binocular performance in clinical tests and its relationship with the interocular symmetry of macular scotomas

We looked at binocular gain for contrast sensitivity and MNREAD acuity in patients with symmetrical and asymmetrical scotomas. Most patients with symmetrical scotomas (66.6%) had no binocular gain in contrast sensitivity, while 33.3% had positive gain. Nobody exhibited evidence of negative gain. Most patients with asymmetrical scotomas (77.7%) had no binocular gain and equal proportions of patients had positive gain and negative gain. There was no significant difference in binocular gain in contrast sensitivity between patients with symmetrical and asymmetrical scotomas.

The majority of patients with symmetrical scotomas (77.7%) had no binocular gain in MNREAD acuity. Equal proportions of patients (11.1%) exhibited positive gain and negative gain. Similarly, most patients with asymmetrical scotomas (72.2%) had no binocular gain, 22.2% had positive gain and only 5.5% had negative gain. Overall, there was no significant difference in binocular gain in MNREAD acuity between patients with symmetrical and asymmetrical scotomas. Hypothesis 5 stated that *clinical performance is expected to be*

superior under binocular viewing conditions compared with the performance using the better eye only in patients with symmetric scotomas. Clinical performance is expected to be equal or worse under binocular viewing conditions compared with the performance using the better eye only in patients with asymmetric scotomas. According to the above results we failed to support hypothesis 5, as we found no significant difference in binocular gain regarding distance and MNREAD acuity and contrast sensitivity between patients with symmetrical and asymmetrical scotomas.

The majority of patients (66.6%) with symmetrical scotomas demonstrated fusion, while only 16.6% with asymmetrical scotomas showed evidence of fusion. There was a significant difference in ability for fusion at the PRL between patients with symmetrical and asymmetrical scotomas, which was in accordance with hypothesis 4.

Although it was also hypothesized that all subjects whose binocular PRLs fell on corresponding retinal location on both eyes and outside the scotomatous areas would retain fusion, only 50% of them reported the perception of a cross during the task; 71.4% of patients with symmetrical scotomas and 33.3% of patients with asymmetrical scotomas. One patient perceived the cross although he was judged to have non corresponding binocular PRLs. Thus, our results failed to support that part of hypothesis 4.

According to these results AMD patients with symmetrical scotomas are more likely to retain fusion compared with patients with asymmetrical scotomas. Schuchard et al (Schuchard et al. 1995) reported that 20% of their patients perceived the target binocularly in a similar task to ours but there was no comment of how much symmetry or asymmetry in macular scotomas there was between the two eyes. Interestingly, they also reported one patient who had binocular perception although he was judged to have no retinal correspondence. Based on the latter fact we could assume that ability for fusion differs in some AMD patients and can possibly exceed the normal recorded motor ranges providing the sensory fusion is intact. Moreover, as we only used an indirect method to locate binocular PRLs locus on the retina, it is likely that there is a component of imprecision in our calculation to account for some of

the discrepancies in our data. More direct techniques such as a binocular SLO would be more likely to provide more accurate information about binocular fixation behavior.

Previous work on eye conditions such as unilateral cataract, longstanding uncorrected unilateral aphakia, or macular diseases such as unilateral macular hole (Mireskandari et al. 2004) has demonstrated impaired fusion in these patients. In such patients fusion is impaired due to the lack of equal binocular sensory input although it has been mentioned that it usually returns once the obstacle to binocular vision has been removed (Pratt-Johnson 1988). Unequal anatomical changes at the retinal area at the two PRLs producing unequal retinal stimulation could be responsible for abnormal sensory fusion (Valberg and Fosse, 2002). These factors could explain the reduced percentage of AMD patients that retain fusion despite the presence of retinal correspondence.

9.4. Conclusions

In summary, AMD patients' fixation stability in the better eye was equal under binocular and monocular viewing conditions while the fixation stability in the worse eye improved under binocular viewing approaching the performance of the better eye. Furthermore, an eyetracker could be used to demonstrate and quantify changes in gaze position and indirectly in retinal location used for fixation in patients with central scotomas due to AMD. We demonstrated that AMD patients did use different PRLs to fixate under binocular versus monocular viewing conditions, especially in cases with asymmetrical scotomas. The fact that the patients changed retinal locations under monocular versus binocular viewing conditions should be taken into account during vision rehabilitation assessments.

In the majority of the cases the binocular fixation loci seemed to fall on retinal areas that could exhibit motor fusion. However, binocular fusion as tested with psychophysical measurements seemed impaired in many AMD patients possibly due to impaired sensory fusion. There was a significant difference in ability for fusion at the PRL between patients with symmetrical and asymmetrical scotomas.

None of the patients showed any evidence of binocular gain for distance acuity. On average, there was no significant difference in binocular gain for contrast sensitivity or MNREAD acuity. However, more patients with symmetrical scotomas had a binocular gain for contrast sensitivity while patients with asymmetrical scotomas were more likely to show a binocular gain for MNREAD acuity.

CHAPTER 10

READING

As was mentioned in the introduction (section 1.3) reading performance, among other tasks, becomes compromised in AMD patients. Many research groups have studied reading and eye movements in AMD using fundus cameras (Nilsson et al. 1998), infrared eye trackers (Bullimore and Bailey 1995), or scleral search coils (Cummings et al. 1985). However, reading performance was mainly measured and analysed monocularly (using the better eye only). As AMD often affects the two eyes differently regarding the size and the location of the scotomas this binocular incongruity may interfere with reading. In this chapter reading performance (reading speed and eye movement parameters) will be compared when using the better eye only versus using both eyes.

Chapter 10 is divided in five main sections. In the first section (10.2.1) reading speed will be measured in the better eye under monocular and binocular viewing conditions when reading orally. In the second section (10.2.2) eye movements during silent reading will be recorded from the better eye under both viewing conditions by means of an infrared eyetracker. The number of forward and regressive saccades used to read a sentence, the number of saccades to find the beginning of the next line, the fixation duration and the saccade size will be evaluated under both monocular and binocular viewing conditions. The importance of these parameters in determining reading speed will also be evaluated in the next section (10.2.3). In section 10.2.4 the predictive role of distance and MNREAD acuity, contrast sensitivity, scotoma size and fixation stability with respect to reading speed will be assessed. Finally, whether clinical measurements (intraocular difference in distance and MNREAD acuity and contrast sensitivity, cover test) and/or psychophysical measurements (binocular PRL location and its correspondence, ability for fusion, symmetrical or asymmetrical macular scotomas) can predict binocular gain in reading speed will be also investigated (10.2.5).

In this chapter hypothesis 6 will be explored (4.2):

Reading speed in patients with symmetric scotomas is expected to be better under binocular versus monocular viewing conditions. In contrast, patients with asymmetric scotomas are expected to behave similarly under monocular and binocular recording conditions.

10.1 Methods

Twenty two patients with bilateral AMD that were included in the previous assessments performed the reading task orally. Of these, nineteen patients also performed the same task silently.

10.1.1. Reading task

The subject was seated 50 cm away from the computer monitor (21" Trinitron GDM-F500R, Sony, Japan) during the test and wore a spectacle correction for this distance (+2.00 dioptres in addition to the distance correction). The background screen luminance was 125cd/m^2, screen resolution was 800x600 pixels and the refresh rate was 70 Hz. Calibration, drift correction and validation were performed using manufacturer's algorithms before initiation of data recording as explained in more detail in section 9.1.1.

Ten sentences were randomly selected from a database of over 500 sentences* that had similar properties to those used on the MNRead card (Legge et al. 1989) in terms of difficulty, length and word order. The sentences had a Flesch-Kincaid Grade level of 4.6. The size of letters used in the text was 3 × distance logMAR acuity. This print size was selected as the minimum acuity reserve reported for "high fluency" reading in macular disease patients is 3:1 (Whittaker and Lovie-Kitchin 1993; Lovie-Kitchin et al. 2000; Massof 2003). When binocular recording was performed, binocular distance acuity was used to determine the size of the text. The sentences were arranged in two lines, left justified in the centre of the screen without splitting words. The font type used was Times New Roman with black letters on a white background.

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* *Sentences were supplied by Dr Elisabeth Fine of Harvard Medical School, Mass., USA. Sentences containing US spelling were removed.*

Initially, each subject was instructed to read each sentence orally with both eyes followed by reading with the better eye (the fellow eye was occluded) or vice versa in random order. The same procedure was repeated again in random order except that the subject had to read the text silently with both eyes and with the better eye.

10.1.2. *Data analysis*

Reading time was calculated in msec for each sentence, when the patient read the text orally, using external computer software (Eyelink Data Viewer software, Version 1.0). Reading time was converted to reading speed in words per minute (wpm) using the formula 600000 / (time in msec).The mean values of reading speed for all ten sentences for each patient were obtained under both viewing conditions. Regression analysis was used to investigate whether reading speed measured monocularly was a good predictor of the reading speed under binocular viewing conditions.

Reading parameters, such as number of forward saccades and regressions, numbers of saccades to find the next line, fixation duration and saccade size were measured during silent reading for both monocular and binocular viewing conditions. Paired t tests were used to compare binocular to monocular performance for all the aforementioned reading parameters. In addition, regression analyses were used to explore whether any of the above parameters were good predictors of reading speed and to assess if clinical and psychophysical measurements such as distance and MNREAD acuity, contrast sensitivity, scotoma size and fixation stability could predict patients' reading speed accurately.

The difference between binocular and monocular reading speed was also computed. We refer to this as binocular gain. Linear regression analyses were used to determine whether the intraocular differences in acuity (distance or reading) and contrast sensitivity were predictive of binocular gain. In addition, the ability to fuse, the location of binocular PRLs, and the presence of symmetrical or asymmetrical scotomas were evaluated in order to explain binocular versus monocular reading speed.

10.2 Results

10.2.1. Reading speed during monocular and binocular recordings

Better eye reading speed is plotted against binocular reading speed for each subject in figure 10.1. There was a good correlation between the reading speed in the better eye under binocular versus monocular recording conditions ($r=0.93$, $p<0.0001$). The slope of this line is 1.0 indicating that the reading speed in the better eye changes by one unit for every unit change of the reading speed under binocular viewing. As the intercept of line is 5.1 it seems that there is a small advantage of 5.1 words /min when reading binocularly. The results of the reading speed for all AMD subjects are presented in detail in table 10a in appendix 2.

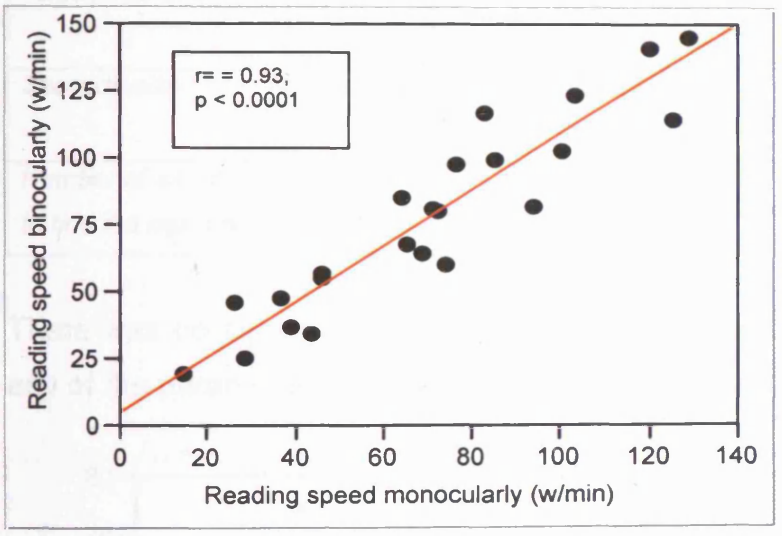

Figure 10.1. Reading speed (in words per minute) during monocular reading (with the better eye only) against reading speed under binocular viewing conditions for all tested AMD patients. The red line represents the best fit linear regression line.

10.2.2. Eye movements during silent reading under monocular versus binocular recordings

The number of fixations and regressions were measured during silent reading. Saccade size (in degrees of visual angle) and duration of fixation were also calculated for both monocular and binocular viewing conditions. The results are presented in detail in table 10a in appendix 2. The mean values, the standard errors of these measurements and paired t-tests results are presented in table 10.1.

Table 10.1. Mean values and SE (standard error) of number of fixations and regressions, fixation duration, saccade size (in degrees of visual angle) and number of saccades to find the beginning of the next line are presented for binocular and monocular viewing during silent reading. Results of paired t-tests are presented in the last column.

	Monocular viewing	**Binocular viewing**	**Paired t test: p- values**
Number of forward saccades	29.6 ± 2.8	29.6 ± 3.2	p=0.66
Number of regressions	10.3 ± 1.0	10.1 ± 0.8	p=0.74
Fixation duration	281.7± 11.9	270.1 ± 12.9	p=0.21
Saccade size	2.8± 1.0	2.4± 1.0	p=0.34
Number of saccades to find the next line	2.3 ± 0.1	2.3 ± 0.2	p=0.91

There was no significant difference between monocular and binocular data for any of the parameters (at the $p<0.05$ level) (Figure 10.2- 10.6).

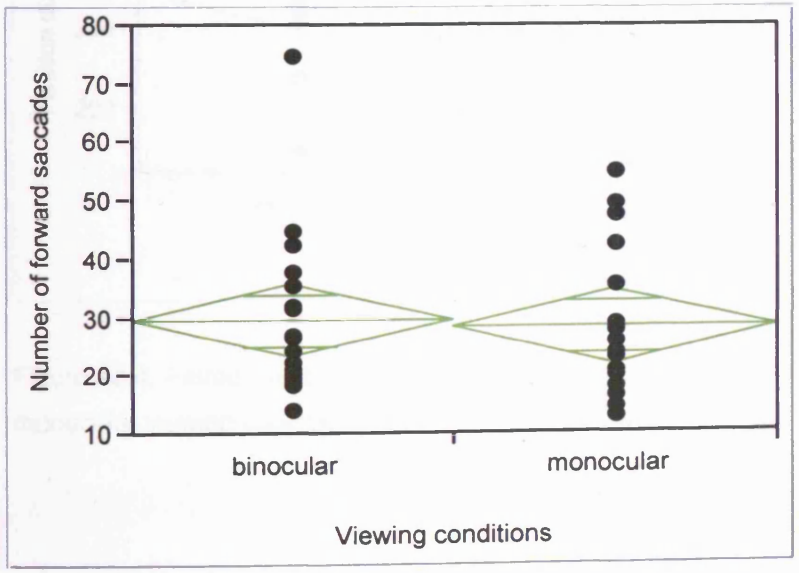

Figure 10.2. Paired t test for number of forward saccades of the better eye under binocular versus monocular viewing conditions. The line across each diamond represents the group mean. The vertical span of each diamond represents the 95% confidence interval for each group.

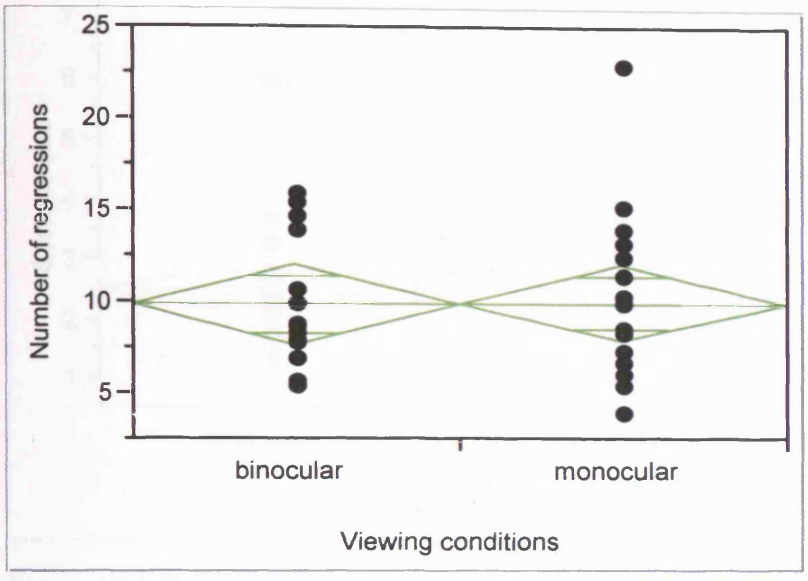

Figure 10.3. Paired t test for number of regression saccades of the better eye under binocular versus monocular viewing conditions.

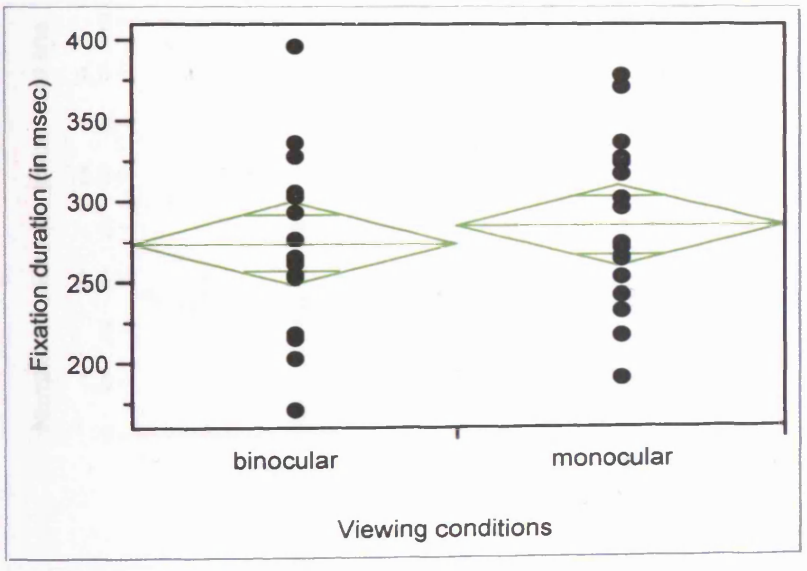

Figure 10.4. Paired t test for fixation duration (in msec) of the better eye under binocular versus monocular viewing conditions.

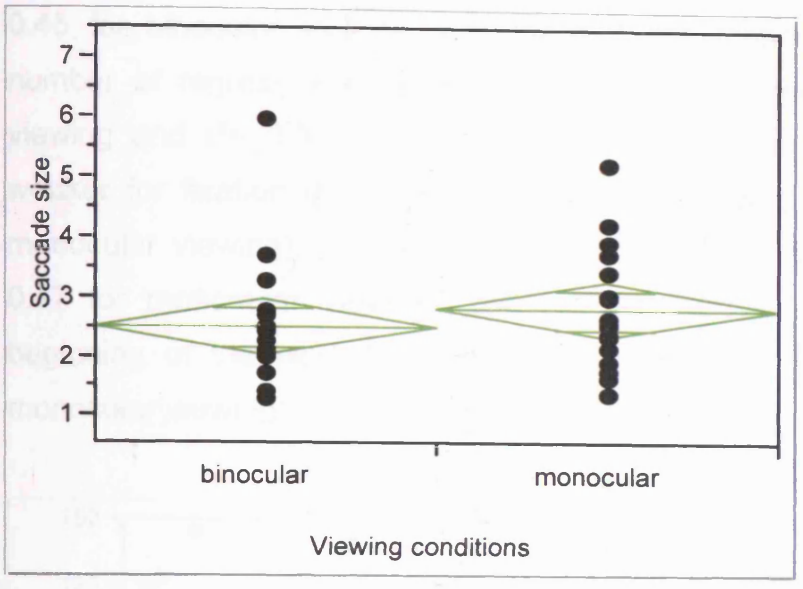

Figure 10.5 Paired t test of saccade size (in degrees per forward saccade) of the better eye under binocular versus monocular viewing conditions.

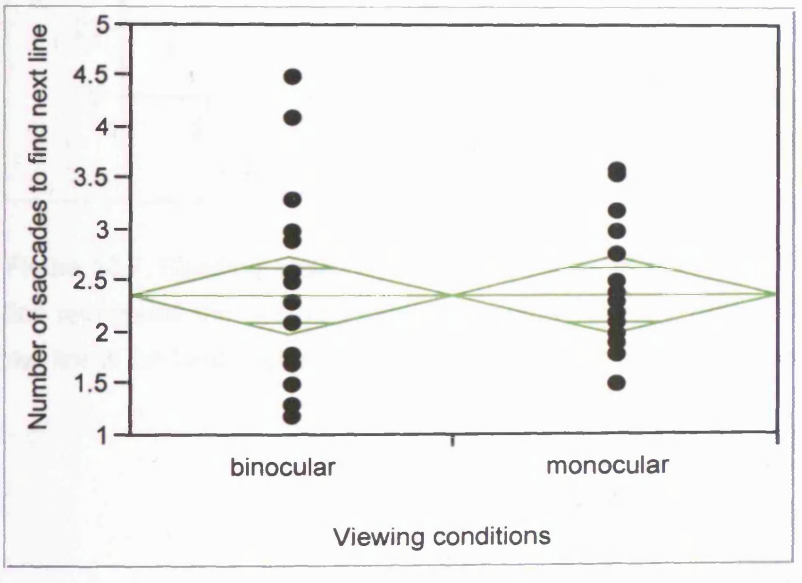

Figure 10.6. Paired t test for number of saccades to find the beginning of the next line of the better eye under binocular versus monocular viewing conditions.

10.2.3. The relationship between eye movements and reading speed

We also investigated whether any of these parameters were related to reading speed. Regression analyses were performed separately for binocular and monocular viewing (figure 10.7-10.11). The number of forward saccades was strongly associated with the reading speed under both viewing conditions (r^2=

0.45 for binocular viewing and r^2= 0.58 for monocular viewing), while the number of regressions was less strongly associated (r^2= 0.15 for binocular viewing and r^2= 0.38 for monocular viewing). The associations were much weaker for fixation duration (r^2= 0.04 for binocular viewing and r^2= 0.01 for monocular viewing), for saccade size (r^2= 0.01 for binocular viewing and r^2= 0.17 for monocular viewing) and for the number of saccades to find the beginning of the next line (r^2= 0.11 for binocular viewing and r^2= 0.16 for monocular viewing).

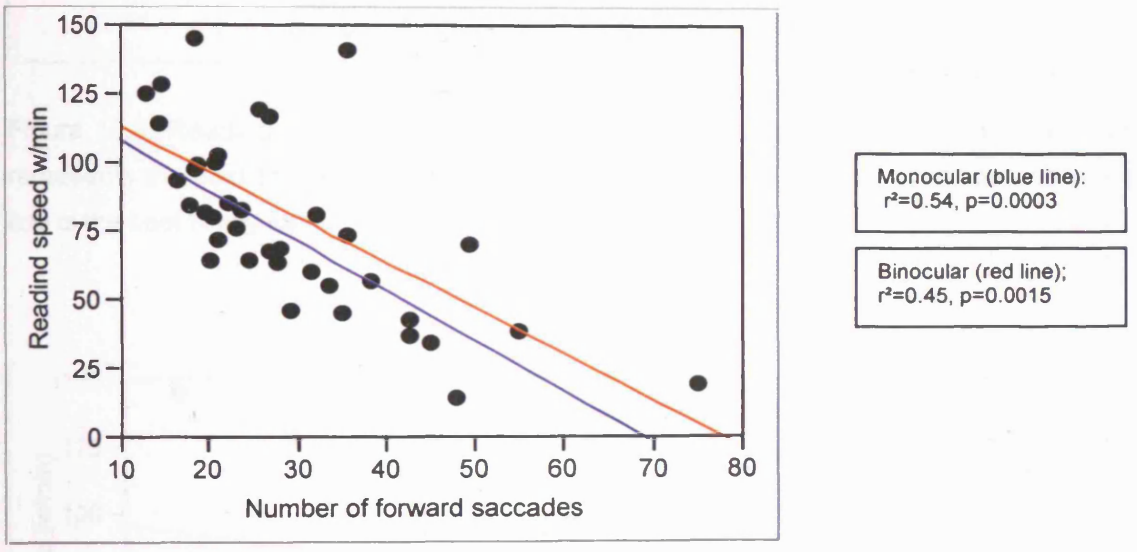

Figure 10.7. Reading speed (in words/min) against the number of forward saccades. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing conditions.

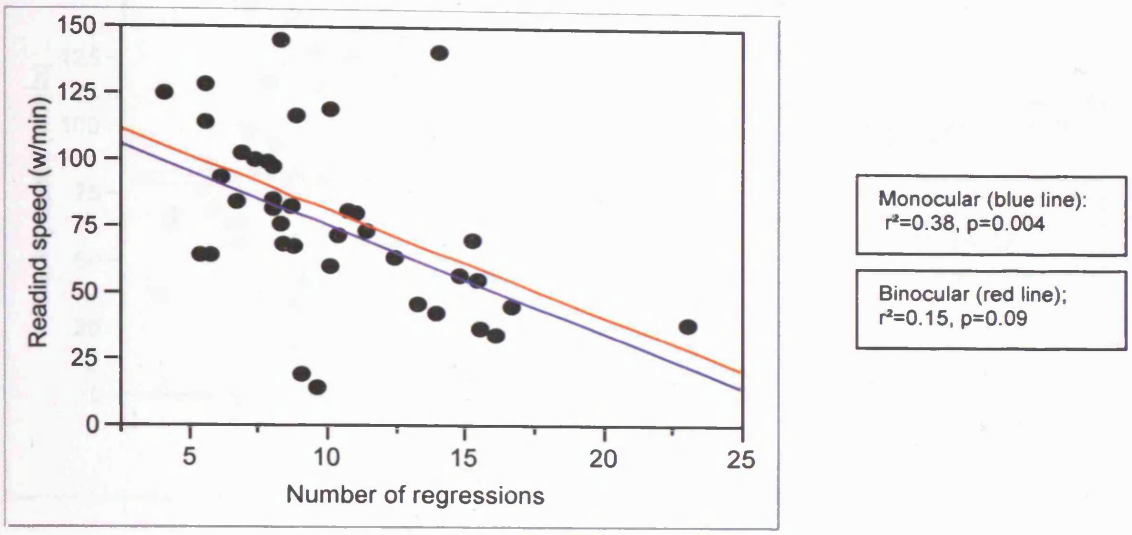

Figure 10.8. Reading speed (in words/min) against the number of regressions. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing conditions.

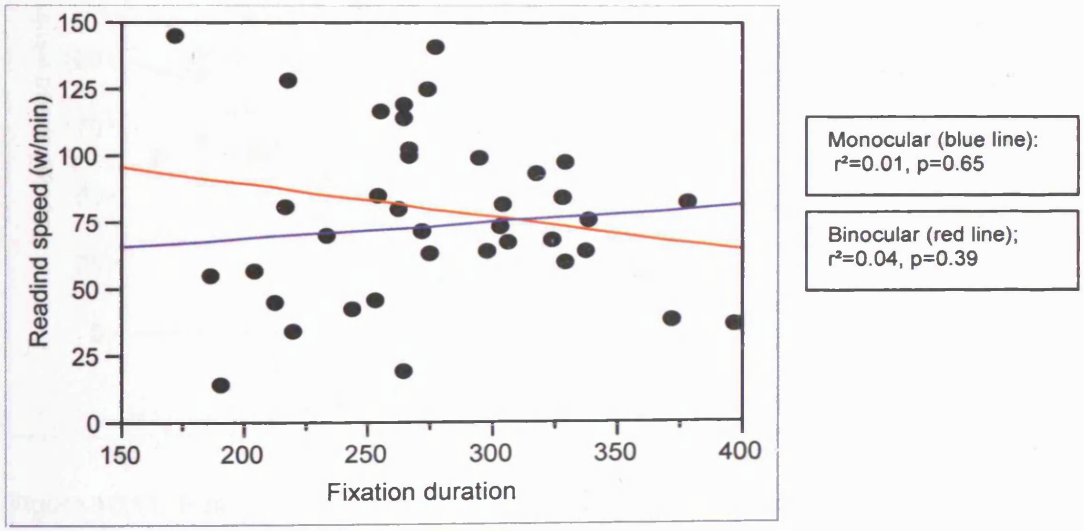

Figure 10.9. Reading speed (in words/min) against fixation duration. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing conditions.

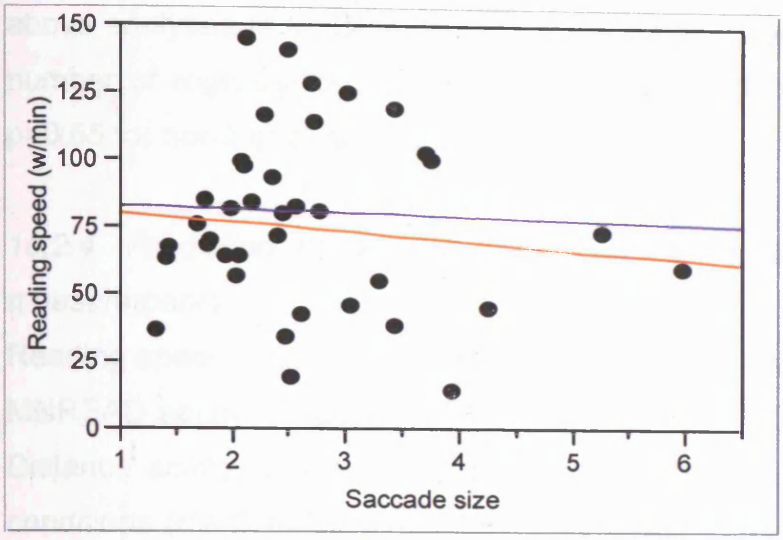

Figure 10.10. Reading speed (in words/min) against saccade size. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing condition.

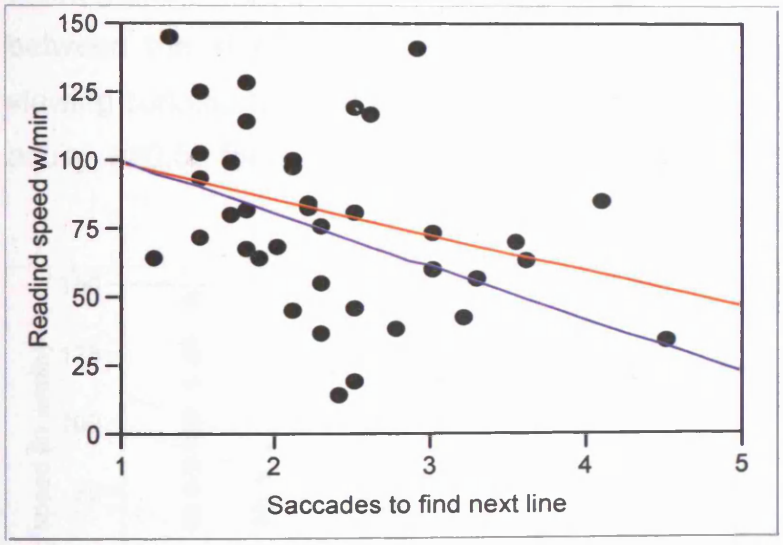

Figure 10.11. Reading speed (in words/min) against number of saccade to find the beginning of next line. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing condition.

Overall, the number of forward saccades was the best predictor of reading speed. We observed stronger associations between reading speed and reading parameters (number of forward saccades, number of regressions, saccade size and number of saccades to find next line) when reading monocularly with the better eye than when reading with both eyes. However, using analysis of covariance (ANCOVA), we found that the slopes of the regression lines for binocular and monocular viewing were not significant different for any of the

above analyses (ANCOVA; p=0.78 for number of forward saccades, p=0.99 for number of regressions, p=0.35 for fixation duration, p=0.85 for saccade size, p=0.65 for number of saccades to find next line).

10.2.4. Prediction of reading speed based on clinical and psychophysical measurements

Reading speed is plotted against distance visual acuity, contrast sensitivity and MNREAD acuity in figure 10.12-10.14 under monocular and binocular viewing. Distance acuity was a strong predictor of reading speed under both viewing conditions (r^2= 0.40 for binocular viewing and r^2= 0.35 for monocular viewing), while MNREAD acuity was just a somewhat weaker predictor of reading speed (r^2= 0.29 for binocular viewing and r^2= 0.27 for monocular viewing). The correlations were much weaker for contrast sensitivity (r^2= 0.03 for binocular viewing and r^2= 0.10 for monocular viewing). There was no significant difference between the slopes of the regression lines under monocular and binocular viewing conditions for any of the above analyses (ANCOVA; p=0.68 for distance acuity, p=0.59 for contrast sensitivity and p=0.71 for MNREAD acuity).

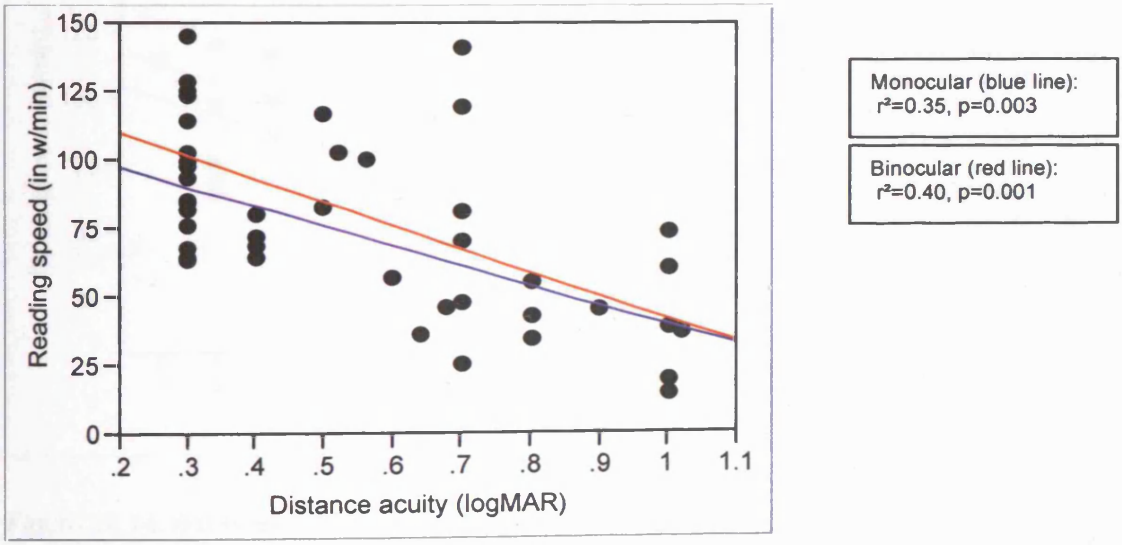

Figure 10.12. Better eye distance visual acuity (in logMAR) against its reading speed (in w/min). The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing conditions.
The red line represents the best fit linear regression line.

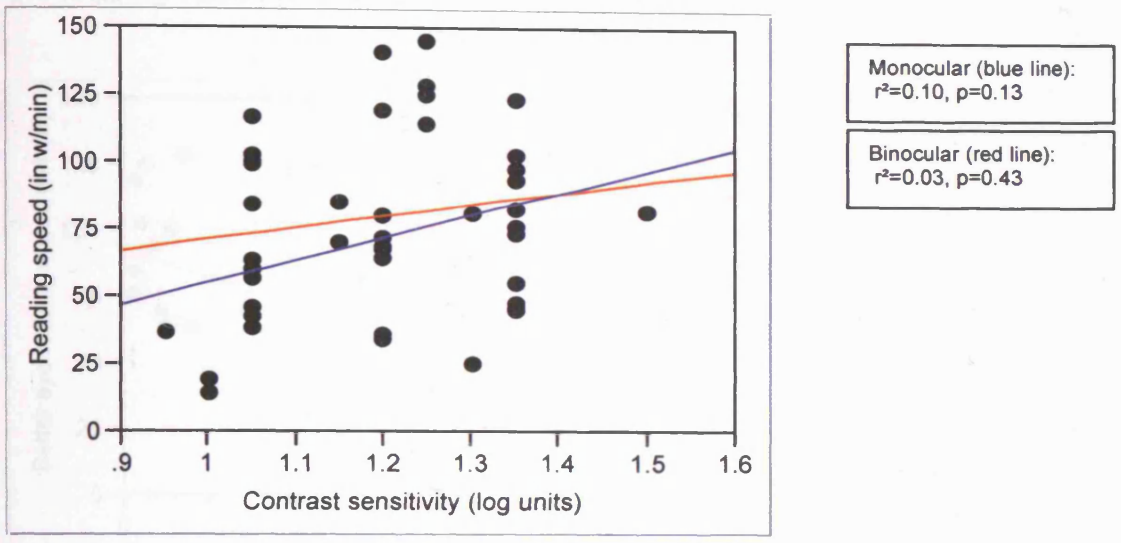

Figure 10.13. Better eye contrast sensitivity (in log units) against its reading speed (in w/min). The red line represents the best fit linear regression line. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing conditions.

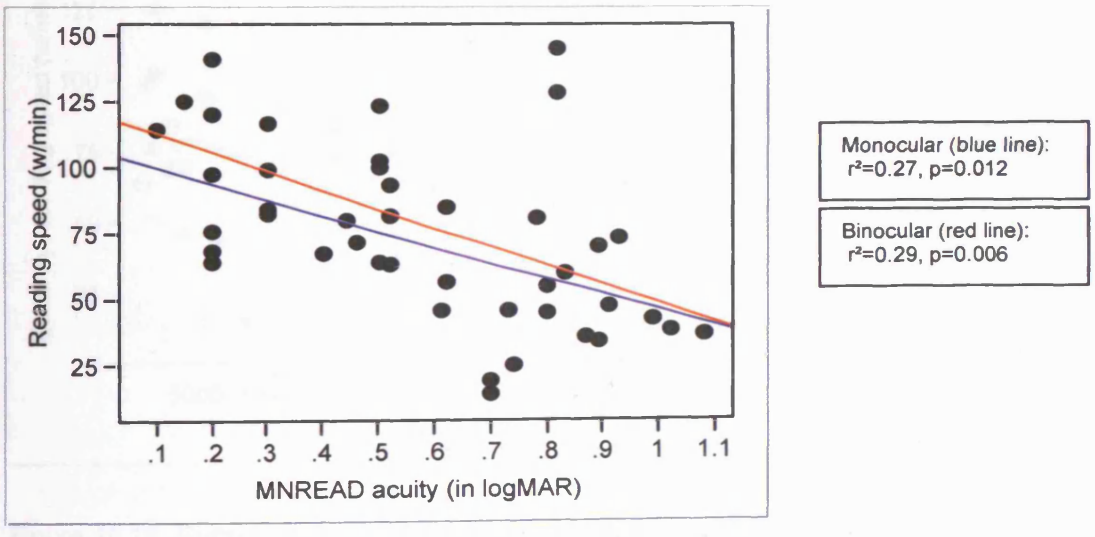

Figure 10.14. Better eye MNREAD acuity (in logMAR) against its reading speed (in w/min). The red line represents the best fit linear regression line. The blue line represents the best fit linear regression line under monocular viewing conditions while the red line is the best fit regression line under binocular viewing conditions.

Scotoma size and fixation stability of the better seeing eye are plotted against the reading speed of the better eye in figure 10.15- 10.16.

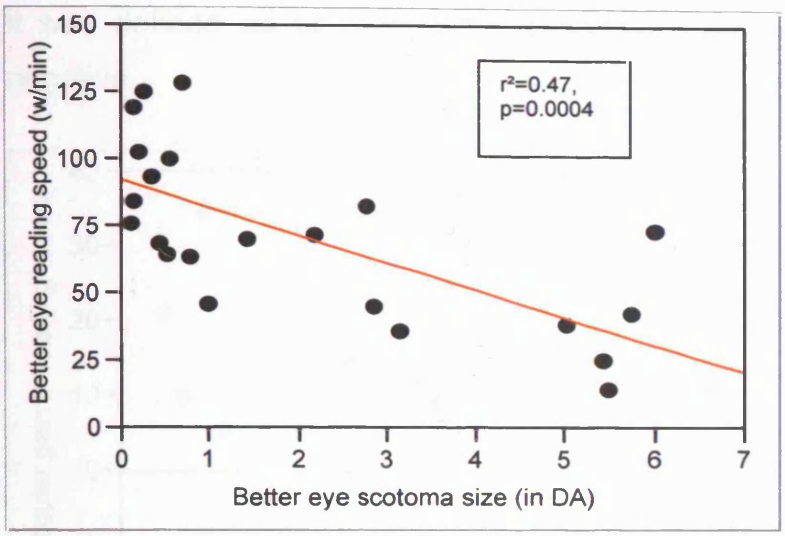

Figure 10.15. Better eye scotomas size (in disc areas) against its reading speed (in w/min). The red line represents the best fit linear regression line.

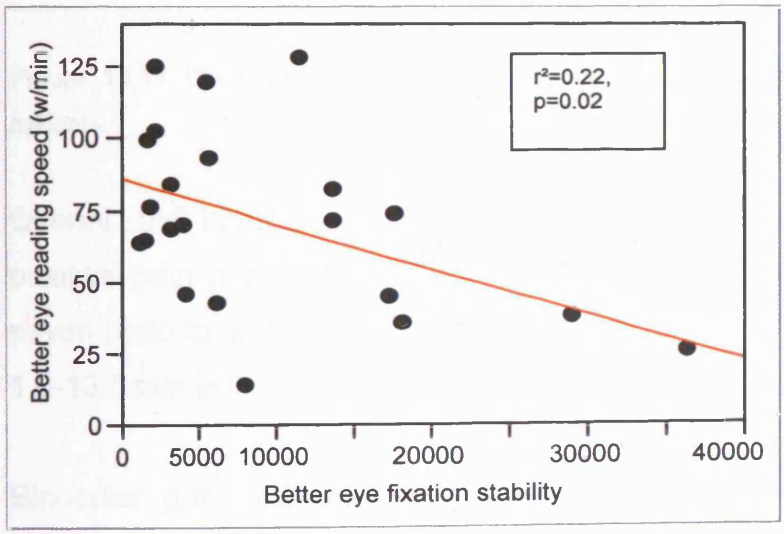

Figure 10.16. Better eye fixation stability (min of arc^2) against its reading speed (in w/min). The red line represents the best fit linear regression line.

Scotoma size was a relatively good predictor of the reading speed (r^2 = 0.47) while fixation stability was a poor predictor of reading speed (r^2 = 0.22).

10.2.5. Prediction of binocular gain- Clinical and psychophysical measurements

The difference between binocular and monocular reading speed (binocular gain) is plotted in figure 10.17. When the binocular gain was above the zero line it was defined as positive; while binocular gain below zero was defined as negative.

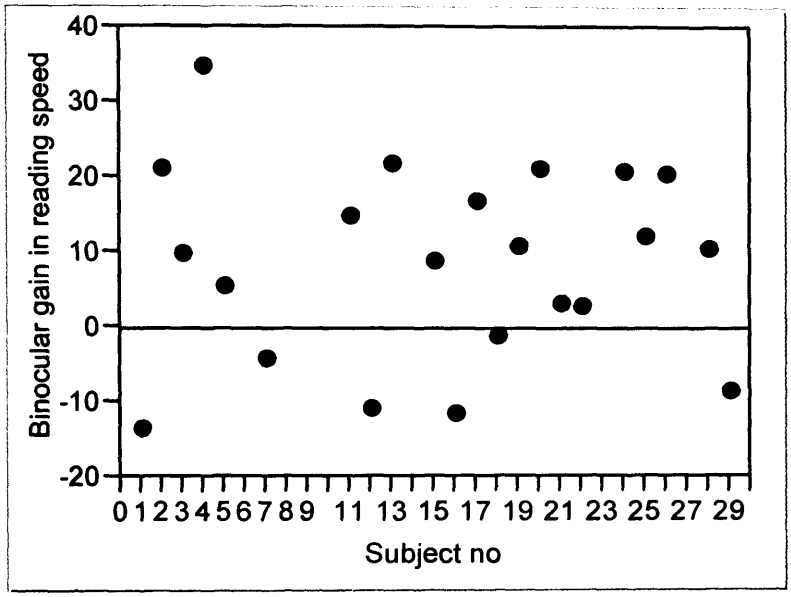

Figure 10.17 Binocular gain in reading speed (in words/min) is plotted for all tested AMD patients.

Overall, the binocular gain was greater than 0. Sixteen patients showed a positive gain (mean gain= 14.7 ± 8.4 SD w/min, range= 2.7- 34.9 w/min) and seven patients showed a negative gain (mean gain=8.2 ± 4.7 SD w/min, range= 1.0-13.5 w/min).

Binocular gain is plotted against the intraocular difference in distance and MNREAD acuity and contrast sensitivity in figures 10.18-10.20.

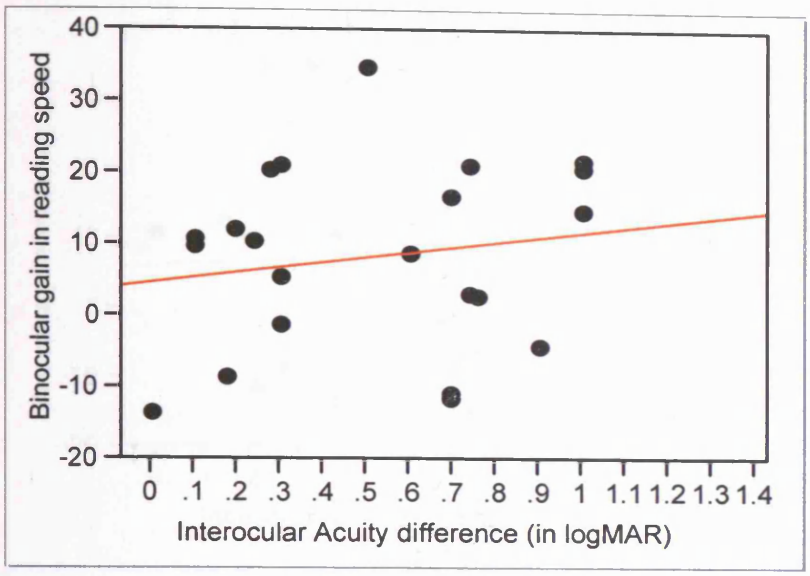

Figure 10.18. Binocular gain (in reading speed (in words/ min) is plotted against the interocular difference in distance acuity (in logMAR) for all tested patients. The red line represents the best fit linear regression line.

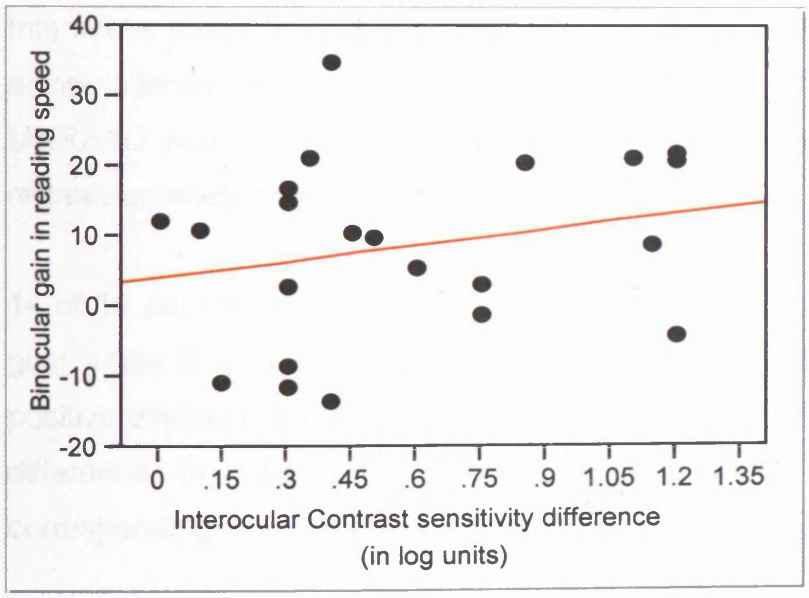

Figure 10.19. Binocular gain (in reading speed (in words/ min) is plotted against the interocular difference in contrast sensitivity (in log units) for all tested patients. The red line represents the best fit linear regression line.

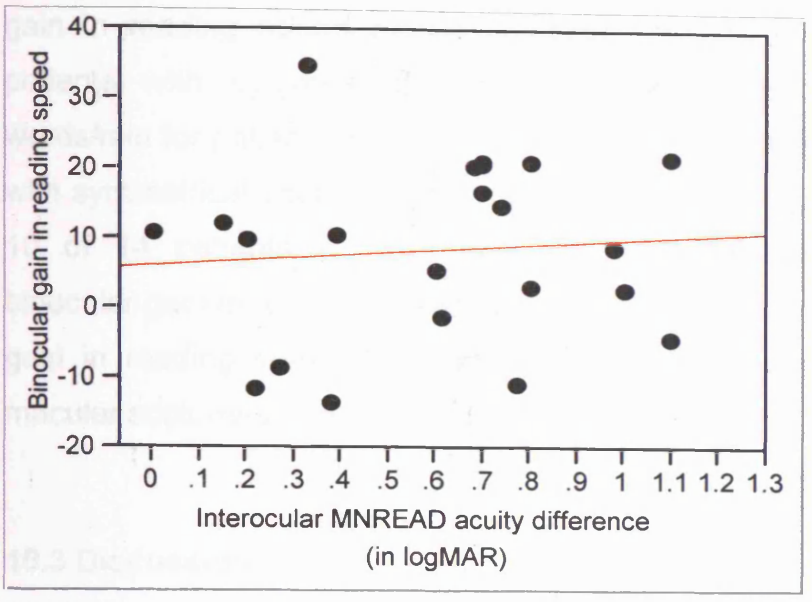

Figure 10.20. Binocular gain (in reading speed (in words/ min) is plotted against the interocular difference in MNREAD acuity (in logMAR) for all tested patients. The red line represents the best fit linear regression line.

Interocular differences were poor predictors of binocular gain (r^2 =0.03 for visual acuity differences, r^2 =0.05 for contrast sensitivity differences and r^2=0.009 for MNREAD acuity differences. However, it was interesting to note that all the regression lines have positive slopes.

14 of 19 patients (73.6%) with corresponding PRLs showed positive binocular gain while 2 of 3 patients (66.7%) with non corresponding PRLs showed positive binocular gain in reading speed. Chi-square test showed no significant difference in binocular gain in reading speed between patients with corresponding and non corresponding PRLs (p=0.80).

In addition, three of six patients (50%) who exhibited fusion at their PRL showed positive binocular gain in reading speed and the same percentage of patients who failed to fuse the target showed positive binocular gain, indicating the ability for fusion at the PRL does not influence binocular gain in reading speed.

We also investigated whether patients with symmetrical macular scotomas were more likely to have a positive binocular gain in reading speed compared with patients with asymmetrical scotomas. Both groups showed a positive binocular

gain in reading speed (mean binocular gain =7.9 ± 14.1SD words/min for patients with symmetrical scotomas; mean binocular gain= 9.4 ± 11.3 words/min for patients with asymmetrical scotomas). Six of eight patients (75%) with symmetrical scotomas had positive binocular gain in reading speed, while 10 of 14 patients (71.5%) with asymmetrical scotomas showed positive binocular gain in reading speed. There was no significant difference in binocular gain in reading speed between patients with symmetrical and asymmetrical macular scotomas (Chi-square test, p=0.85)

10.3 Discussion

All AMD patients included in this study showed almost equal reading speed under binocular and monocular viewing conditions. There was only a small advantage of 5.1 words/ min for binocular reading, on average.

There was no significant difference in the number of forward saccades, the number of regressions, the fixation duration, the saccade size, or the number of saccades to find the beginning of the next line during silent reading with both eyes versus better eye only. Furthermore, the number of forward saccades was a good predictor of reading speed for both viewing conditions (r^2= 0.45 for binocular viewing and r^2= 0.58 for monocular viewing) but the other eye movement variables were poorer predictors of reading speed. Overall, we found no significant difference in the predictive value of these variables on reading speed during reading with the better eye versus with both eyes.

Our results are consistent with previous studies. McMahon et al. found a somewhat higher correlation (r=-0.79) between reading speed and saccadic frequency, which was a comparable measurement to the number of forward saccades, although they used five spaced letters in sequence as a reading text instead of a standardised text (McMahon et al. 1991; McMahon et al. 1993) and their patients had received training. Bowers et al also reported a very strong correlation between reading speed and number of saccades (r= -0.97) (Bowers et al. 2001). Bullimore and Bailey (Bullimore and Bailey 1995) reported a correlation of 0.86 to 0.96 (depending on the luminance levels used). They suggested three critical factors that could have influenced that behaviour.

Firstly, they claimed that as the visual span was reduced in AMD fewer letters could be read in each fixation. Furthermore, the ability to direct the eyes to the required part of the text and to integrate information within and across sequential information were both impaired in AMD patients. All of these factors could partially explain why AMD patients demonstrated more forward saccades while reading and consequently read slower.

We found that reading speed could not be accurately predicted by fixation duration (r^2= 0.04 for binocular viewing and r^2= 0.01 for monocular viewing), saccade size (r^2= 0.00 for binocular viewing and r^2= 0.01 for monocular viewing) and the number of saccades to find the beginning of the next line (r^2= 0.11 for binocular viewing and r^2= 0.16 for monocular viewing). Previous data on fixation duration showed that fixation duration was linearly related to the reading speed in subjects with simulated visual impairment (r=-0.86) (Bowers and Reid 1997). However, Bullimore and Bailey (Bullimore and Bailey 1995) reported no correlation between reading speed and fixation duration in AMD subjects. Moreover, he reported that their fixation duration was equal to the fixation duration of the control subjects (around 300msec), which was consistent with our results (mean fixation duration under monocular reading was 281.7 msec ± 11.9 SD; mean fixation duration under binocular reading was 270.1 msec ± 12.9). Regarding saccade size they reported in the same paper their results from two AMD patients. The patient with the better performance (larger saccade size) read about 3.5 letters per forward saccade size, which converts to about 175 min of arc per forward saccade for print size 1.0 logMAR. These values were similar to ours (mean saccade size: 2.8° ± 1.0° SD for monocular viewing and 2.4° ± 1.0° SD for binocular viewing), although we measured saccade size with character spaces (including the space between words) instead of letters per forward saccade.

Distance and MNREAD acuity were better predictors of reading speed than contrast sensitivity (for distance acuity r^2= 0.40 for binocular viewing and r^2= 0.35 for monocular viewing; and for MNREAD acuity r^2= 0.29 for binocular viewing and r^2= 0.27 for monocular viewing). There was no significant difference between the slopes of the regression lines under monocular and binocular viewing conditions for any of the clinical tests. Similar results for distance acuity

were reported by Sunness et al (Sunness et al. 1996) (r^2 =0.43). Fletcher et al (Fletcher et al. 1999) and Legge et al (Legge et al. 1992) also showed similar results (r^2 values of 0.32 and 0.33 respectively). In accordance with previous reports, we also found that scotoma size was a good predictor of the reading speed (r^2= 0.47). Previous work in this area showed r^2 values to vary between 0.23-0.45 (Cummings et al. 1985; Sunness et al. 1996; Fletcher et al. 1999; Ergun et al. 2003).

We also found that fixation stability was a poor predictor of reading speed (r^2= 0.22). Crossland (Crossland 2004d) reported a similar correlation between the two of them in patients with newly acquired macular disease (r^2 = 0.21 at the onset of visual loss and 0.26 after one year).

The majority of patients (72.2%) showed a positive binocular gain in reading speed. However, binocular gain could not be predicted by the intraocular differences in distance and MNREAD acuity or contrast sensitivity. However, it was interesting to note that all the regression lines for acuity (distance and MNREAD) and contrast sensitivity had positive slopes. An explanation for this behaviour could be that a possible inhibitory effect of the worse eye on the performance of the better eye, that was exhibited when the two eyes were similar, was repressed when acuities or contrast sensitivities were very different in the two eyes. Thus, binocular reading speed and therefore, binocular gain would increase as the intraocular difference in clinical tests becomes larger.

Most patients (73.6%) with corresponding PRLs showed positive binocular gain and only the minority of patients (33.3%) with non corresponding PRLs showed negative binocular gain in reading speed. Therefore, the presence of retinal correspondence at the PRLs did not play a role in binocular gain. The ability for fusion at the PRL does not influence binocular gain in reading speed as the same number of patients showed positive or negative gain among the ones who fuse and the ones who did not fuse the target. The above results could be explained by the fact that AMD patients could use a different PRL to perform the fixation tasks and different PRL or even multiple PRLs during reading text (Deruaz et al. 2002).

Contrary to hypothesis 6, we found no difference in binocular gain in reading in patients with symmetrical and asymmetrical scotomas.

10.4. Conclusions

Reading speed when using both eyes was highly correlated with the reading speed for the better eye, and although there was a small advantage of binocular viewing, binocular reading speed could be accurately predicted by the reading speed of the better eye.

There was no difference in eye movements (number of forward saccades and regressions, fixation duration, saccade size, and number of saccades to find the beginning of the next line) with both eyes versus better eye. A good correlation was found between reading speed and the number of forward saccades, while the correlation was less strong for the number of regressions. The correlation was weaker for the other eye movement parameters (fixation duration, saccade size and number of saccades to find the beginning of the next line). Scotoma size, distance and MNREAD acuity were good predictors of reading speed compared with fixation stability and contrast sensitivity, which were proven poor predictors of reading speed. Overall, there was no significant difference between binocular and monocular reading for any of the above regression analyses.

Most of the AMD patients showed a positive binocular gain in reading speed. Interocular differences in clinical measurements did not affect binocular gain in reading speed. The majority of patients with corresponding PRLs showed positive binocular gain. However, the ability for fusion at the PRL does not influence binocular gain in reading speed. Finally, there was no difference in binocular gain with respect to reading speed between patients with symmetrical and asymmetrical macular scotomas and therefore, our data failed to support hypotheses 6 regarding reading performance.

DICUSSION AND CONCLUSIONS

CHAPTER 11

GENERAL DISCUSSION AND CONCLUSIONS- IMPLICATIONS FOR FUTURE RESEARCH

In this chapter we will discuss the principal findings of this project in relation to the hypotheses defined in chapter 4. The limitations of this study will be also raised and further discussed. Finally, the main conclusions of this project and their implications for future research will be also outlined.

Age related macular degeneration is a bilateral eye condition with high rates of symmetric manifestations between the two eyes in the early or end-stage of the disease, as previously reported (Chuang and Bird 1988; Wang et al.1998; Lavin et al. 1991; Bellmann et al 2002). However, both eyes are not often affected simultaneously. A clinical study has commented on an asymmetry of macular lesions due to a different degree of foveal sparing between the two eyes at the earlier stages of the disease, especially in cases of geographic atrophy (Sunness et al. 1996). Moreover, often, even at the end stage of the disease, some degree of asymmetry in the retinal lesions between the two eyes can be clinically observed. Although it is expected that bilateral involvement will be increased with age, because of the aforementioned factors most AMD patients experience some degree of asymmetry in macular lesions during the course or the end stage of the disease. In a cross section study of AMD patients coming to medical retina clinics at Moorfields Eye Hospital only 1/3 of the recruited patients had symmetrical scotomas according to our definition (interocular difference in scotomas size ≤ 1 disc area). However, we acknowledge the fact that it is likely that our patients may not be representative of the proportion of the symmetry or asymmetry of the disease in the general AMD population, as patients with more advanced disease in one eye tend to attend the clinics more, being anxious about second eye involvement, than patients with advanced disease in both eyes, where patients are aware that treatment options are not yet available.

During this project we investigated the impact of the symmetry of macular scotomas on monocular versus binocular viewing during fixation and reading and the potential of binocular function in AMD patients.

11.1 Monocular viewing: monocular PRLs and macular scotomas

11.1.1 Location of monocular PRLs

We found that most patients fixated below or to the left of the scotomas in visual field space which is in accordance with previous reports (White and Bedell 1990; Guez et al. 1993; Sunness et al. 1996; Fletcher and Schuchard 1997; Nilsson et al. 1998; Fletcher et al. 1999). Few patients (3%) fixated with their better eye on a normal central retinal area surrounded by multiple small scotomatous areas in cases of geographic atrophy. However, some patients (12%) placed their PRL on a possible island of vision within the scotomatous area mainly in their worse eye. Most of our AMD patients placed their PRL very close to the borders of the scotomas in accordance with previous reports (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999) and in contrast to patients with juvenile macular disease, where they tend to fixate further away from the scotomas edges.

11.1.2 Monocular PRLs, retinal correspondence and symmetry of macular scotomas

In AMD patients in general, fixation locus seemed to shift to the site of retina closest to the fovea (Tezel et al. 1996). We found that scotoma size was a good predictor of retinal eccentricity of the monocular PRL with respect to the normal fovea (r^2= 0.49). However, despite the presence of symmetrical scotomas there was a difference in foveal sparing between the two eyes in some of our patients that affected PRL position, as was mentioned earlier. This gave rise to a fixation area with a very close proximity to the fovea despite the presence of an absolute scotoma. Other researcher groups (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999) have also reported that, especially in cases of geographic atrophy, patients initially develop a atrophic lesion in a horseshoe appearance with sparing of the fovea. In addition, we found that some of our patients fixated within an island of presumed normal retinal function within the scotomatous area and thus, the distance of their PRL to the fovea did not show a good correlation with the scotoma size. The presence of additional anatomic

abnormalities not mapped as 'absolute' scotomas could also cause further shift of the PRL to more peripheral locations. Although scotoma size was a better predictor of the eccentricity of the PRLs' position in the better eye compared to the worse eye there was no significant difference between these two regression lines.

We found a significant association (r^2= 0.38) between interocular differences in scotomas size and difference in eccentricity of monocular fixation locus between the two eyes. Only 1/3 of our AMD patients demonstrated symmetrical scotomas in the two eyes. We found that patients who had symmetrical scotomas showed significantly smaller distances between their monocular PRLs (mean distance between the two loci: 3.2° ± 1.4° SD), compared to patients with asymmetrical scotomas (mean distance: 8.9° ± 4.8° SD) and therefore, similar retinal eccentricities. Overall, more patients with symmetrical scotomas (30%) were using corresponding monocular PRLs compared to patients with asymmetrical scotomas (5.5%).

In hypothesis 1 it was stated that *AMD patients with symmetrical central scotomas would be more likely to have preferred retinal loci with similar retinal eccentricities in both eyes under monocular viewing conditions than patients with asymmetrical scotomas. Therefore, their PRL in the two eyes would be more likely to fall on more corresponding retinal areas than in patients with asymmetrical scotomas.* Our results were in accordance with hypothesis 1.

11.1.3. Prediction of distance visual acuity, contrast sensitivity and MNREAD acuity from scotoma size and retinal eccentricity of PRL

Retinal eccentricity of PRL position and scotoma size were relatively good predictors for distance acuity (r^2= 0.26 in both cases), when the PRL was located within 4 degrees from the fovea and the scotoma size was less than 4 disc areas. For eccentricity greater than 4 degrees visual acuity reached a plateau at 0.9 logMAR, while for scotomas greater than 4 disc areas distance acuity reached a plateau with only slight deterioration with further increase in scotoma size.

In accordance with our results, previous papers have documented that visual acuity in AMD patients is worse at their fixation locus than was expected from normal data for that eccentricity (Brown et al. 1984; White and Bedell 1990; Tezel et al. 1996; Rees et al. 2004). It has been suggested that the PRL used during SLO recordings was not the same as the one used to measure acuity on the clinical test (ETDRS chart) and this could explain the published data. However, the visual acuity measured with the SLO and ETDRS chart showed minimal difference (Guez et al. 1993; Sunness et al. 1996; Fletcher et al. 1999), which was suggestive of the fact that patients are likely to be using the same fixation to perform the clinical test and the SLO task. One alternative hypothesis was that the presence of multiple anatomic anomalies (detachment of the retinal pigment epithelium, subretinal haemorrhage, RPE atrophy) could further affect the visual acuity at the fixation locus and account for those results. Guez et al (Guez et al. 1993) proposed that AMD patients preferred to use a less eccentric position as the pseudo-fovea, in a part of the retina which maybe not completely healthy, rather than going further into peripheral retina with better acuity. Ludvigh reported that retinal eccentricity of 4 degrees in normal subjects has visual acuity of 0.5logMAR (Ludvigh 1941), while in our AMD patients visual acuity was measured at 0.9 log MAR for that eccentricity. However, in their better eye visual acuity was 0.6 log MAR and thus very close to normal values. We found that the correlation between eccentricity of the PRL and visual acuity was significantly better in the better eye compared with the worse eye.

We also found that scotoma size was a significantly better predictor of distance acuity for the better eye compared with the worse eye. Other researchers have also documented the fact that although there was high symmetry of retinal lesions between the two eyes, there was a large variation in the visual acuity between the better and the worse eyes. They attributed this firstly to a different degree of foveal sparing between the two eyes and secondly to a possible suboptimal use of the remaining functional retina in the worse eye (Sunness et al. 2000). In support of these hypotheses was the fact that an improvement in the visual acuity in the worse seeing eye could be observed when the better seeing eye began to deteriorate (Sunness et al. 2000).

Regarding contrast sensitivity, we found that eccentricity of the PRLs and scotoma size had no predictive effect. Although the correlations were better for the better eye compared to the worse eye neither of them reached good predictive values.

We reported that retinal eccentricity of PRL position was a relatively weak predictor for MNREAD acuity for any eccentricities, while scotoma size was a relatively good predictor of MNREAD acuity. Ergun et al. (Ergun et al. 2003) reported similar a correlation between reading acuity and absolute scotoma size. However, both the eccentricity of the PRL and scotoma size were good predictors for MNREAD acuity only for the better eye but not for the worse eye. We found significant difference in the above correlations between the better and the worse eye for both scotoma size and eccentricity of the PRL.

11.1.4. Limitations

For this study, we defined retinal corresponding points as those which, when simultaneously stimulated, give rise to the percept of a single object (Millidot, Dictionary of Optometry). The distances between the two monocular PRLs for all subjects exceeded the amount that could be explained by Panum's area. However, as the distance between the monocular PRLs was measured based on indirect methods (initially identification of the centre of the blind spot on the SLO image, then superimposition of the distance from the centre of the blind spot to fovea as measured in normal subjects, and consequently evaluation of the distance between the monocular PRLs used by the two eyes during SLO recordings) there was an unavoidable degree of measurement error in our data as mentioned earlier. When measurement errors were taken into account, four patients were still considered to be using non corresponding retinal areas when viewing monocularly.

11.1.5. Implications

The main conclusion from this part of the thesis is that more patients with asymmetrical retinal lesions demonstrated PRLs that fell on non corresponding retinal areas under monocular viewing conditions compared to patients with symmetrical disease. Based on these results many questions have been raised. As Raasch speculated in his paper we could anticipate that patients either use

both non corresponding points under binocular viewing conditions in a reading task, shift attention between those PRLs, experience confusion, or simply suppress one PRL (Raasch 2004). As we have already demonstrated in chapter 9, some patients can alternatively choose another fixation locus when viewing binocularly. Therefore, assessment of their monocular fixation behaviour is not always enough to draw conclusions about binocular viewing.

As all the associations between scotoma size and eccentricity of the PRL and distance and MNREAD acuity are strong only for the better eye but not for the worse eye, questions have been raised about how accurate these clinical measurements are when tested the worse seeing eye. Previous authors have suggested a suboptimal use of the remaining functional retina in the worse eye (Sunness et al. 2000). We agree with them and we think that one of the reasons to account for the large variation in the measurements between the better and the worse eye is the fact that when we ask the patient to perform a test monocularly with his worse seeing eye, we force them to use a retinal locus that they do not really use under the natural binocular viewing conditions. We don't really know what their selection criteria are, assuming they are not chosen by chance, and how consistent this behaviour is. Testing the repeatability of these measurements will probably shed more light on these issues.

It is also interesting that the selection criteria for treatment for AMD patients (e.g. NICE *guidelines for Photodynamic Therapy*) are partially based on the results from acuity charts during monocular viewing conditions. If the eye for potential treatment is the first eye, it is very likely that acuity will be worse compared to what is expected from that given scotoma size or retinal eccentricity of the locus they are using to perform the task. In that respect we are probably prone to treat patients with better acuities than the ones measured. On the other hand when the second eye involvement is more severe than the first eye, it is unlikely that treatment of the second eye would manifest any improvement, and therefore the effect of the treatment will be underestimated.

Furthermore, in cases of asymmetrical retinal disease such as in unilateral macular holes the effectiveness of possible intervention won't be so accurately

evaluated as the preoperative measurements are likely to be worse than expected compared to the size of the scotomas and therefore, the magnitude of the benefit could be overestimated.

These considerations also apply for visual acuity measurements during low vision assessment of AMD patients.

11.1.6. Conclusions

Most AMD patients fixated below or to the left of the borders of the scotomas in visual space, and scotoma size was a good predictor of retinal eccentricity of PRL location.

Only one third of our patients had symmetrical scotomas. There was a significant correlation between interocular differences in scotomas size and difference in eccentricity of monocular fixation locus between the two eyes. A difference in foveal sparing in the two eyes and the presence of additional anatomic abnormalities not mapped as 'absolute' scotomas may have prevented a better correlation. Monocular PRLs seemed to fall on more corresponding retinal areas in patients with symmetrical scotomas compared to patients with asymmetrical scotomas.

Scotoma size was a better predictor of the eccentricity of the PRLs' position in the better eye compared with the worse eye but there was no significant difference between them. Both retinal eccentricity of PRL position and scotoma size were good predictors of distance and MNREAD acuity only in the better eye but weak predictors of contrast sensitivity in both eyes.

11.2. Monocular versus binocular viewing: fixation stability, shift in gaze position and binocular PRLs

11.2.1. Fixation stability

Fixation stability was impaired, on average, in our AMD patients but there was large inter-subject variability in BCEA size. We recorded larger values than previous reports (Culham et al. 1993; Schuchard and Fletcher 1994 ;

Rohrschneider et al. 1995; Tezel et al. 1996; Nilsson et al. 1998; Crossland and Rubin 2002), firstly because we used an eyetracker for our recordings, which allows free head movement and increases BCEAs compared to SLO and secondly, because we included recording from the worse eye as well. Nevertheless, we believe that the eyetracker is a better instrument than the SLO to evaluate fixation stability, as it allows recording under more natural viewing conditions. As we found no significant difference in fixation stability when patients were using the better eye or both eyes to fixate the target, we concluded that patients' fixation stability in the better eye was very similar under both viewing conditions. However, fixation stability improved significantly in the worse eye when the subject was viewing binocularly compared to monocular viewing. There was a good correlation between the binocular BCEA in both eyes ($r=0.76$). These results indicated that binocular fixation stability is mainly driven by the 'better' eye. The worse eye did not seem to affect (inhibit) the performance of the better eye during binocular recording, but it appeared rather to follow the fixation pattern of the better eye and therefore, improved its binocular BCEA.

In this study we found that distance and MNREAD acuity were good predictors of the size of BCEAs in the better eye ($r^2=0.42$ for distance acuity and $r^2=0.50$ for MNREAD acuity) but not in the worse eye. Contrast sensitivity was a poor predictor of the BCEA in both eyes. The difference in the correlations between the better and the worse eye were significant for both measurements. This difference is mainly due to the fact that even for comparatively good acuities, the size of the BCEA in the worse eye was relatively large (figure 9.2 and 9.2.4). The fact that the worse eye was forced under the testing conditions to fixate monocularly with a PRL that in some cases has not used before under the natural binocular viewing conditions (chapter 9) could explain why its fixation stability was so poor compared to the better one. Crossland et al. showed poor correlations between the size of BCEA and both distance acuity and contrast sensitivity ($r=0.33$ for distance acuity and $r= 0.00$ for contrast sensitivity), even when he tested the better eye. However, he examined a different group of patients from ours, as he evaluated patients with newly acquired macular disease for both AMD and juvenile cases (Crossland et al.

2004b) and thus their behaviour could be different from patients with more stable disease, as in the present study.

11.2.2. Changes in gaze position

82.7% of our AMD patients demonstrated a shift in their gaze position either in one eye or both eyes, when they changed from monocular to binocular viewing during a fixation task. There was a significant difference in the shift distance between the better and worse eye with the smaller shift recorded in the better eye. As the median of the shift in the gaze position in the better eye was 2.5°, which approached our definition of a normal shift (2.3°), it indicated that the better eye kept its gaze position or changed less than the worse eye when switching from monocular to binocular viewing of the target.

The cover test identified most of the patients who used different areas to fixate when viewing binocularly versus monocularly. The cover test is a quick and useful clinical procedure for assessing gaze position but as its accuracy depends on the examiner's experience, the eyetracker could be used as an alternative for more objective and accurate documentation of changes in gaze position, which is needed for further evaluation of binocular behaviour in these patients.

AMD patients that were using the same PRLs to fixate under monocular versus binocular viewing conditions demonstrated fusion near their PRLs. Only the minority of patients who showed a shift either in one or both eyes retained fusion at the fixation loci indicating that either fixation loci fell within the scotomas in the worse eye or retinal correspondence was disrupted and fusion was inhibited.

There was significant difference between patients with symmetrical and asymmetrical scotomas with respect to the shift in gaze position. More patients with symmetrical scotomas (almost half of them) showed no shift in gaze position compared to patients with asymmetrical scotomas (22.3%) According to hypothesis 2 in *patients with symmetrical scotomas no shift in gaze position is expected from monocular to binocular viewing. Therefore, patients are expected to use the same PRLs under both viewing conditions in both eyes.*

However, patients with asymmetrical scotomas are expected to use different PRLs under binocular versus monocular viewing at the worse eye. A shift in the PRL locus is expected in the worse eye under binocular versus monocular viewing conditions. Therefore, our data partially support hypothesis 2.

11.2.3. Binocular PRLs, retinal correspondence and ability for fusion

As far as we are aware there are only very limited reports of binocular viewing in AMD patients (Schuchard and Fletcher 1994; Schuchard et al. 1995; Schuchard et al. 2003). Schuchard et al. (Schuchard and Fletcher 1994; Schuchard et al. 1995) first reported that some AMD subjects may use monocular PRLs that fall on non corresponding retinal areas. By using an SLO for monocular recordings combined with a psychophysical task to test binocular perception of the target they concluded that binocular fixation tasks were driven by the 'dominant' eye. More recently, the same group attempted to produce binocular SLO results by combining monocular SLO data but, as they indicated, the main limitation was the inability to accurately predict gaze position in binocular viewing (Schuchard et al. 2003).

Our hypothesis 3 predicts that *AMD patients will exhibit PRLs under binocular viewing conditions with similar retinal eccentricities between the two eyes. These PRLs are likely to fall on corresponding retinal areas in the two eyes. No difference is expected in patients with symmetrical versus asymmetrical scotomas with respect to retinal correspondence of binocular PRLs.*

Overall, most of AMD patients were using PRLs under binocular viewing conditions whose distances could be explained by measurement errors. Only 14.8% of our patients (two patients with symmetrical scotomas and two patients with asymmetrical scotomas) demonstrated differences in the PRLs that were outside these measurements and suggested that these patients maybe used non corresponding binocular PRLs. No difference in the distance between the binocular PRLs was found between patients with symmetrical and asymmetrical scotomas, which is in accordance with hypothesis 3.

Furthermore, a significant difference was found when the distances between the two monocular PRLs were compared to the distances between the two binocular PRLs in patients with asymmetrical scotomas but not when compared

in patients with symmetrical scotomas, indicating that binocular PRLs seemed to fall on more corresponding retinal areas compared to the monocular ones in the two eyes.

Schuchard et al (Schuchard et al. 1995) reported a lower percentage of retinal correspondence compared to our results. In specific, they concluded that only 40% of their patients (versus 85.2% in our study) had retinal correspondence of their binocular PRL in both the horizontal and vertical directions, 10% only vertically, none horizontally and 50% in neither direction. However, in their study, retinal correspondence was judged based on the location of the monocular PRLs as identified using an SLO and the assumption of patients using the same monocular and binocular PRLs was made. Furthermore, correspondence was measured based on the interocular difference in retinal distances between the physiological blind spot and the PRL, although it was not mentioned in their paper how they determined retinal correspondence of the PRLs based on their calculations.

Although, binocular fusion was preserved in all recruited patients' according to the results of the Bagolini test, only 33% of them demonstrated fusion at their PRL using the psychophysical task (chapter 7). Most patients with symmetrical scotomas demonstrated local fusion, while only the minority of patients with asymmetrical scotomas showed evidence of local fusion. Therefore, there was a significant difference in ability for local fusion at the PRL between patients with symmetrical and asymmetrical scotomas, which was in accordance with hypothesis 4. Furthermore, it has been hypothesized that all subjects whose binocular PRLs fell on corresponding retinal loci in both eyes and outside the scotomatous areas should retain local fusion. We found that only 50% of them reported fusion during the task; 71.4% of patients with symmetrical scotomas and 33.3% of patients with asymmetrical scotomas. One patient perceived the cross although he was judged to have non corresponding binocular PRLs. Thus, our results failed to support the part of hypothesis 4.

According to these results AMD patients with symmetrical scotomas are more likely to retain fusion compared with patients with asymmetrical scotomas. There is very limited reported data on fusion in AMD patients. Schuchard et al

(Schuchard et al. 1995) reported that 20% of their patients perceived the target binocularly in a similar task to ours but there was no comment of how much symmetry or asymmetry in macular scotomas there was between the two eyes. Interestingly, they also reported one patient who had binocular perception although he was judged to have no retinal correspondence. Based on the latter fact we could assume that ability for fusion differs in AMD patients and can possibly exceed the normal recorded ranges. More direct techniques such as a binocular SLO would be more likely to provide more accurate information about binocular fixation behavior.

Previous work on eye conditions such as unilateral cataract, longstanding uncorrected unilateral aphakia, or macular diseases such as unilateral macular hole (Mireskandari et al. 2004) has demonstrated impaired fusion in these patients. In such patients fusion is impaired due to the lack of equal binocular sensory input although it has been mentioned that it usually returns once the obstacle to binocular vision has been removed (Pratt-Johnson 1988). Unequal anatomical changes at the retinal area at the two PRLs producing unequal retinal stimulation could be responsible for abnormal sensory fusion (Valberg and Fosse, 2002). These factors could explain the reduced percentage of AMD patients that retain fusion despite the presence of retinal correspondence.

11.2.4. Limitations

As for monocular PRLs we used the same definition for retinal corresponding points for binocular PRLs. We defined retinal corresponding points as those which, when simultaneously stimulated, give rise to the percept of a single object (Millidot, Dictionary of Optometry). The distances between the two binocular PRLs for all subjects exceeded the amount that could be explained by Panum's area. . However as the retinal location for the binocular PRLs was measured based on indirect methods (through eyetracker recordings for fixation data and the results superimposed on SLO pictures), there was an unavoidable degree of measurement error in our data as mentioned earlier. When the total measurement errors were taken into account most of these distances could be explained due to these errors and only four patients were considered to be using non corresponding retinal areas when viewing binocularly.

Moreover, one possible limitation of this study is the fact that although we had no independent evidence of heterotropia for any of our patients according to our results we found that a few patients were using non corresponding PRLs, and therefore, should have some squint.

Moreover, the fusional ranges within Panum's area were based on examination of normal sighted observers and the reported ranges were measured on patients that at least fixated with the fovea in one eye. We have no reported data to describe fusion ranges when both eyes are using peripheral retinal loci to fixate. We can only make the assumption that different rules may apply for AMD patients with bilateral disease. Based on the fact that fusional ranges increase with retinal eccentricity, the ability to fuse images in the retinal periphery using other fixation loci than the fovea could be enhanced. Yet, fusional ranges could be abnormal in AMD patients, as previous investigators have reported abnormal values for other patients with macular diseases such as unilateral macular holes (Mireskandari et al. 2004).

11.2.5. Implications

We demonstrated that although information about monocular behaviour is valuable it does not necessarily provide a useful insight into how people with bilateral scotomas operate in the real world as AMD often presents with variable degrees of incongruity between the two eyes with respect to the size, location and density of the scotomas. Therefore, it was not surprising to find that monocular PRLs were located in non corresponding retinal areas. The eye tracker data helped to address this problem albeit by providing indirect information about the retinal location used during fixation. When the patient viewed binocularly, one or both of the monocular PRLs were ignored due to the need to find a binocularly useful retinal area. Subsequently, overriding conjugate eye movements were engaged. In addition, a few subjects demonstrated a shift in both eyes, possibly searching for an appropriate gaze position in order to fixate on a functional retinal area that could be used binocularly. Despite the conflicting views whether training of AMD patients using their optimal PRLs can improve their performance (Culham et al. 1997; Nilsson et al. 1998; Nilsson et al. 2003), it is generally believed that the development of appropriate eccentric viewing seems to be critical for effective visual

rehabilitation. If binocular PRLs are at different locations from monocular PRLs, patients' binocular behaviour should be studied in a more detailed way to aim for successful rehabilitation and advice for these patients should be based on the individual performance.

We used the term "binocular PRL" to define the fixation locus used in both eyes under binocular viewing condition. Up to now the term "PRL" was mainly used only under monocular viewing conditions, and moreover, to define a retinal area that was chosen, consciously or unconsciously to fixate a target. As we showed in this project, many of our patients, especially in their worse eye, demonstrated a shift, which was driven by their better eye as the latter one did not change its fixation. So the worse eye just followed the better eye, as the better eye was taking up fixation. Furthermore, in a few subjects, the PRL under binocular viewing conditions fell within the scotomatous area and therefore no image was perceived at that locus. In that respect, this fixation area could not be termed as the "preferred" retinal area for fixation of the worse eye. It was a retinal area that was the focus of attention fell due to the conjugate eye movements of the two eyes. Thus, it was more a 'conventional' than a preferred retina area that was used. The term 'binocular preferred retinal loci' have been previously used by Schuchard et al (Schuchard et al. 1995), but after the results of this study the term should be revisited for binocular conditions. However, in cases where there was a shift in both eyes under binocular versus monocular viewing, this term could be more appropriate, as it appeared that there was a possible compromise from both eyes in order to find a binocular functional retinal area to fixate.

Raasch in his recent editorial (Raasch 2004) raised the question whether suppression of one PRL occurs when there is non correspondence. We know from this study that one reason for lack of fusion in AMD cases is the fact that PRLs fell within the dense scotomas in the worse eye especially in the presence of asymmetrical scotomas. We also showed that there were cases that demonstrated non corresponding binocular PRLs that could explain the lack of ability for fusion, although we don't know exactly how these PRLs could be used together as the patient did not have a manifest squint. Although this was only one case, we would suggest that ability for fusion in AMD patients

may follow different rules and fusional ranges could be different than the ones we used to compare our results. In cases of corresponding retinal points that fell outside scotomas, where there was no recorded ability for fusion, the possibility of impaired sensory fusion due to the presence or relative scotomas could be hypothesized. However, suppression cannot be excluded.

11.2.6. Conclusions

AMD patients do often use different PRLs to fixate under binocular versus monocular viewing conditions, especially in cases with asymmetrical scotomas. An eyetracker can be used to demonstrate and quantify changes in gaze position and indirectly in retinal location used for fixation in patients with central scotomas due to AMD The fact that the patients do change retinal locations under monocular versus binocular viewing conditions should be taken into account during vision rehabilitation assessments. However, binocular fusion as tested with psychophysical measurements seemed impaired in some AMD patients possibly due to impaired motor and/ or sensory fusion.

11.3. Monocular versus binocular performance in clinical tests

The results from the monocular versus binocular performance in clinical tests have been presented in chapter 7.

In general, AMD patients showed equal binocular performance to the performance of the better eye alone with respect to clinical tests such measurements of distance and MNREAD acuity and contrast sensitivity. Moreover, binocular acuity could be predicted from monocular acuity, which was in accordance with previous reports (Rubin et al. 2000). Interocular differences in acuities did not play any role with respect to binocular gain in distance visual acuity. Similar results were obtained for all the above observations regarding contrast sensitivity and MNREAD acuity.

Rubin et al. (Rubin et al. 2000) showed that in older normal patients with equal acuities in the two eyes the binocular summation for visual acuity on average was only 0.03 logMAR or 1.5 letters and in AMD cases they reported little

evidence for binocular inhibition when the monocular acuities in the two eyes were unequal, which is in agreement with our data.

Most of our AMD subjects demonstrated no improvement in their performance when viewing binocularly versus monocularly with the better eye with respect to contrast sensitivity. We found a benefit in binocular viewing for 20% of the patients, while 6.65% of AMD patients showed binocular inhibition. More specifically, when the interocular difference in sensitivity was greater than 0.40 log units there was no binocular gain. If the difference was equal or less than this the majority of patients (46.1%) showed a small positive gain (mean positive gain was 0.15 log units) and 15.38% of patients showed negative gain (mean negative gain was 0.3 log units). However, in both cases the binocular gain was relatively small.

It has been previously reported that when there are unequal monocular contrast sensitivities such as in cataract or in amblyopia reduced binocular summation (Pardhan and Gilchrist 1991; Pardhan and Gilchrist 1992) can occur. Therefore, evidence of binocular inhibition was expected in AMD patients, where unequal retinal stimulation had been expected, especially in patients with asymmetrical disease. This lack of binocular summation and the presence of inhibition regarding contrast sensitivity in AMD patients have previously been reported (Fosse et al. 2001). Our results showed a lower percentage of inhibition in AMD patients than previously recorded. Valberg and Fosse (Valberg and Fosse 2002) demonstrated reduced binocular summation while 61% of his AMD patients showed binocular inhibition. Faubert and Overbury (Faubert and Overbury 2000) also reported a high percentage (almost 50%) of AMD showing binocular inhibition regarding contrast sensitivity. This "inhibition" was not related to the contrast sensitivity of the better eye or to the visual acuities and it was more obvious primarily in images with medium to low spatial frequency components.

Overall, only 16.6% of AMD patients showed binocular summation in their MNREAD acuity, while 6.6% of patients showed binocular inhibition. Interocular differences played no role in binocular gain. Nevertheless, despite the binocular outcome, the overall binocular gain, positive or negative was very small for

MNREAD acuity (mean positive gain 0.10 logMAR and mean negative gain 0.17 logMAR).

When we evaluated binocular versus monocular performance with respect to the symmetry of macular scotomas (section 9.3.5.) we found the following results: more patients had a positive binocular gain of patients with symmetrical scotomas compared to patients with asymmetrical scotomas (33.3% versus 11.1%), but the difference was not statistically significant. Nobody exhibited evidence of negative gain of patients with symmetrical scotomas but 11.1% of patients with asymmetrical scotomas showed a negative binocular gain. Thus, there maybe some benefit in binocular viewing regarding contrast sensitivity, mainly in cases with symmetrical macular disease, especially during some every day tasks such as seeing steps, curbs, irregularities in the pavement etc. that depend on contrast detection but the potential benefit should be assessed on an individual basis.

On average, there was no significant difference in binocular gain in MNREAD acuity between patients with symmetrical and asymmetrical scotomas. However, more patients with asymmetrical scotomas had a positive gain compared to patients with symmetrical scotomas (22.2% versus 11.1%). Additionally, more patients with symmetrical scotomas had a negative gain compared to patients with asymmetrical scotomas (11.1% versus 5.5%). These results indicating that MNREAD acuity may occasionally benefit from binocular viewing more in patients with asymmetrical scotomas than in patients with symmetrical scotomas. We have no good explanation for these results.

Hypothesis 5 stated that c*linical performance is expected to be superior under binocular viewing conditions compared with the performance using the better eye only in patients with symmetric scotomas. Clinical performance is expected to be equal or worse under binocular viewing conditions compared with the performance using the better eye only in patients with asymmetric scotomas.* According to the above results we found no binocular gain regarding distance acuity and furthermore, there was no significant difference in binocular gain in

contrast sensitivity and MNREAD acuity between patients with symmetrical and asymmetrical scotomas. Thus, we failed to support hypothesis 5.

Previous studies of normally sighted people with simulated poor acuity showed good stereovision with Snellen acuity ≥ 6/18 in both eyes (Donzis et al. 1983). Equal vision in the two eyes was more important than the absolute level of vision in either eye and three lines of acuity difference between the two eyes would disrupt stereoacuity (Rubin et al. 1997). There are only limited studies of stereoacuity in patients with retinal and optic nerve disorders, which showed a disproportionately greater reduction in their stereoacuity compared to what it was expected from the normal nomograms (Friedman et al. 1985; Shah et al. 1995). According to Shah et al. patients with Snellen acuity no better than 20/30 in even one eye are likely to have abnormal stereoacuity. Although none of our subjects had distance visual acuity better than 0.3 log MAR (equivalent to 6/15 Snellen acuity) in both eyes and at the same time less than three lines of acuity difference between the two eyes, nevertheless we decided to test stereoacuity in our subjects. And, indeed, none of our AMD patients demonstrated any level of stereoacuity. Valberg and Fosse (Valberg and Fosse 2002) proposed that the presence of asymmetrical macular scotomas leading to unequal retinal stimulation is the reason for the reduced binocular acuity, contrast sensitivity and even impaired stereopsis that AMD patients are experiencing.

11.3.1. Implications

It is interesting to note that due to the fact that some AMD patients were using different PRLs to fixate under monocular versus binocular viewing conditions, the binocular performance of their PRLs during a fixation task is not the additive performance of the two monocular ones. For example when we are measuring the distance acuity in each eye monocularly we test PRLs that could be completely different from the ones used during binocular viewing, and therefore, we measured the combined effect of different fixation loci either in both or in one eye when viewing with both eyes. In that respect, it is very difficult to predict patients' binocular performance based on their monocular performances. From that point of view one could assume that assessment of binocular performance should be incorporated in our clinical practice when assessing patients for low vision aids and rehabilitation strategies. However, as

the PRL in cases of asymmetrical scotomas often fell within the scotoma in the worse eye, it is not surprising that binocular performance equals the performance of the better eye and the evidence of binocular summation or inhibition are weak. In such cases, evaluation of the better eye is likely to be a good predictor of the overall binocular performance.

11.3.2. Conclusions

Overall, binocular performance was equal to the performance of the better eye alone. Therefore, estimation of patients' performance could be based on monocular measurements and separate assessment of binocular data is not required.

There was no binocular gain with respect to distance visual acuity. Regarding contrast sensitivity and MNREAD acuity a binocular gain was observed although it was relatively small (either positive or negative gain). For contrast sensitivity the binocular gain was observed only when the interocular difference in sensitivity was equal to or greater than 0.4 log units. There was no similar trend for MNREAD acuity. None of the patients demonstrated any level of stereoacuity.

11.4. Monocular versus binocular reading in AMD patients

Reading speed when using both eyes was highly correlated with the reading speed for the better eye only, and although there was a small advantage in binocular viewing, binocular reading speed could be accurately predicted by the reading speed of the better eye.

There was no difference in eye movements (number of forward saccades and regressions, fixation duration, saccade size, and number of saccades to find the beginning of the next line) with both eyes versus better eye. A good correlation was found between reading speed and the number of forward saccades, while the correlation was less strong for the number of regressions. The correlation was weaker for all the other eye movement parameters (fixation duration, saccade size and number of saccades to find the beginning of the next line). Scotoma size, distance and MNREAD acuity were good predictors of reading

speed compared to fixation stability and contrast sensitivity, which were poor predictors of reading speed.

Most of the AMD patients showed a positive binocular gain in reading speed. Interocular differences in clinical measurements did not affect binocular gain in reading speed. The presence of retinal correspondence of the PRLs in the two eyes and the ability for fusion at the PRL did not influence binocular gain in reading speed.

Hypothesis 6 stated that r*eading speed in patients with symmetric scotomas is expected to be better under binocular versus monocular viewing conditions. In contrast, patients with asymmetric scotomas are expected to behave similarly under monocular and binocular recording conditions.* We found no difference in binocular gain with respect to reading speed between patients with symmetrical and asymmetrical macular scotomas and therefore, our data failed to support hypotheses 6.

11.4.1. Limitations

We used an infrared eyetracker to assess performance in AMD patients because of its high sampling rate and large field of view, which allowed accurate assessment of eye movement parameters. We could alternatively use the SLO to examine which PRL the patients were using during reading but that would have compromised the evaluation of reading parameters as the SLO has a lower sampling rate compared with the eyetracker. Furthermore, using the SLO, there is a limitation to the natural viewing behaviour as patients have to use a chin and a forehead rest and to view the screen from a fixed distance.

11.4.2. Implications

In this study we had few patients (4 patients) that had non corresponding PRLs in the two eyes when viewing binocularly during a fixation task. Although we do not know if they were using the same PRLs during reading, we, like Raasch (Raasch 2004), question whether these PRLs can be both used in a reading task. However, Deruaz et al. (Deruaz et al. 2004) showed that patients can alternate between two retinal locations when deciphering a word. Furthermore, Raasch queried whether it was possible for AMD patients to focus selectively

on one or the other PRL if a word fell simultaneously on both PRLs. The inability of our AMD patients in this project to map their blind spot with the technique described in chapter 6 showed that they probably could not split their attention between a PRL and another peripheral retinal locus. However, we don't know if their behaviour would have been different if that other peripheral locus were a second PRL in cases of multiple PRLs.

Overall, although most of our AMD patients showed a binocular gain in reading speed, overall this gain was small. Moreover, evaluation of reading performance of AMD patients using their better eye is a good predictor of binocular behavior and patients' advice could be based on the monocular performance.

As a general rule in clinical practice when acuities of the two eyes are similar it is considered visually beneficial for the patient to use binocular low vision devices. In cases where acuities are unequal no binocular gain is expected. Another factor that needs to be taken into consideration is the fact that sometimes the design of the magnifying device or the limitation on the viewing conditions which it imposes, makes the use of a binocular device very difficult (Dickinson 1998). Based on the results of this study we did not find any reason to advise patients to use binocular devices for reading. However, if they prefer viewing binocularly, there seems to be no reason to discourage it.

11.4.3. Conclusions

Reading speed when using both eyes could be accurately predicted by the reading speed of the better eye only, although there was a small advantage in binocular viewing (about 5 words/min, on average).

There was no difference in eye movements with both eyes versus better eye. A good correlation was mainly found between reading speed and the number of forward saccades. Scotoma size, distance and MNREAD acuity were good predictors of reading speed, but fixation stability and contrast sensitivity were poor predictors of reading speed. We found no significant difference between binocular and monocular reading for any of the above parameters.

Most of the AMD patients showed a positive binocular gain in reading speed, which cannot be predicted by the interocular differences in clinical measurements. The presence of retinal correspondence in the PRLs between the two eyes and the ability for fusion at the PRL did not affect binocular gain. We found no difference in binocular gain with respect to reading speed between patients with symmetrical and asymmetrical macular scotomas.

In summary, evaluation of reading performance of AMD patients using their better eye is a good predictor of binocular behavior and patients' advice could be based on the monocular performance.

REFERENCES

(1980). "Recommended stardard procedures for the clinical measurement and specification of visual acuity. Report of working group 39. Committee on vision. Assembly of Behavioral and Social Sciences, National Research Council, National Academy of Sciences, Washington, D.C." Adv Ophthalmol **41**: 103-48.

Adler (1987). Adler's Physiology of the eye. St. Louis, The C. V. Mosby Company.

Age-Related Eye Disease Study Research Group (2000). "Risk factors associated with age-related macular degeneration. A case-control study in the age-related eye disease study: age-related eye disease study report number 3." Ophthalmology **107**: 2224-32.

Algvere, P., Berglin, L., Gouras, P. and Sheng , Y. (1994). "Transplantation of fetal retinal pigment epithelium in age-related macular degeneration with subfoveal neovascularization." Graefes Arch Clin Exp Ophthalmol **232**(12): 707-16.

Algvere, P. V., Berglin, L., Gouras, P., Sheng, Y. and Kopp, E. D. (1997). "Transplantation of RPE in age-related macular degeneration: observations in disciform lesions and dry RPE atrophy." Graefes Arch Clin Exp Ophthalmol **235**(3): 149-58.

Anderson, S. J., Mullen, K. T. and Hess, R. F. (1991). "Human peripheral spatial resolution for achromatic and chromatic stimuli: limits imposed by optical and retinal factors." J Physiol **442**: 47-64.

Anzai, A., Bearse, M. J., Freeman, R. and D., C. (1995). "Contrast coding by cells in the cat's striate cortex: monocular vs. binocular detection." Vis Neurosci. **Jan-Feb;12**(1): 77-93.

Arditi, A. (1986). Binocular vision. Handbook of perception and human performance.

AREDS (2001). "A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for agerelated
macular degeneration and vision loss: AREDS report no. 8." Arch Ophthalmol **119**(10): 1417-36.

Bagolini, B. (1985). "Objective evaluation of sensorial and sensorimotorial status in esotropia: their importance in surgical prognosis." Br J Ophthalmol **69**(10): 725-8.

Bailey, I. L., Bullimore, M. A., Raasch, T. W. and Taylor, H. R. (1991). "Clinical grading and the effects of scaling." Invest Ophthalmol Vis Sci **32**: 422-432.

Barondes, M., Pauleikhoff, D., Chisholm, I. C., Minassian, D. and Bird, A. C. (1990). "Bilaterality of drusen." Br J Ophthalmol **74**(3): 180-2.

Bartsch, D. U., Weinreb, R. N., Zinser, G. and Freeman, W. R. (1995). "Confocal scanning infrared laser ophthalmoscopy for indocyanine green angiography." Am J Ophthalmol **120**(5): 642-51.

Beatty, S., Murray, I. J., Henson, D. B., Carden, D., Koh, H. and Boulton, M. E. (2001). "Macular pigment and risk for age-related macular degeneration in subjects from a Northern European population." Invest Ophthalmol Vis Sci **42**(2): 439-46.

Bellmann, C., Feely, M., Crossland, M., Kabanarou, S. and Rubin, G. (2004). "Fixation stability using central and pericentral fixation targets in patients with age-related macular degeneration." Ophthalmology in press.

Bellmann, C., Holz, F. G., Schapp, O., Volcker, H. E. and Otto, T. P. (1997). "[Topography of fundus autofluorescence with a new confocal scanning laser ophthalmoscope]." Ophthalmologe **94**(6): 385-91.

Bellmann, C., Jorzik, J., Spital, G., Unnebrink, K., Pauleikhoff, D. and Holz, F. G. (2002). "Symmetry of bilateral lesions in geographic atrophy in patients with age-related macular degeneration." Arch Ophthalmol **120**(5): 579-84.

Bellmann, C., Miller, D. W., Mehltretter, K., Schutt, F., Jorzik, J., Unnebrink, K. and Holz, F. G. (2003). "Digital analysis of choroidal neovascularisation in consecutive fluorescein angiograms for use in longitudinal clinical trials." Br J Ophthalmol **87**(7): 890-2.

Berger, J. W. (1997). "Thermal modelling of micropulsed diode laser retinal photocoagulation." Lasers Surg Med **20**(4): 409-15.

Bergink, G. J., Hoyng, C. B., van der Maazen, R. W., Vingerling, J. R., van Daal, W. A. and Deutman, A. F. (1998). "A randomized controlled clinical trial on the efficacy of radiation therapy in the control of subfoveal choroidal neovascularization in age-related macular degeneration: radiation versus observation." Graefes Arch Clin Exp Ophthalmol **236**(5): 321-5.

Bettelheim, F. A. and Chylack, L. T., Jr. (1985). "Light scattering of whole excised human cataractous lenses. Relationships between different light scattering parameters." Exp Eye Res **41**(1): 19-30.

Bird, A. C., Bressler, N. M., Bressler, S. B., Chisholm, I. H., Coscas, G., Davis, M. D., de Jong, P. T., Klaver, C. C., Klein, B. E., Klein, R. and et al. (1995). "An international classification and grading system for agerelated maculopathy and age-related macular degeneration. The International ARM Epidemiological Study Group." Surv Ophthalmol **39**(5): 367-74.

Blake, R. (1989). "A neural theory of binocular rivalry." Psychol Rev. **Jan;96**(1): 145-67.

Blake, R. and Fox, R. (1973). "The psychophysical inquiry into binocular summation." Percept Psych. **14**: 161-185.

Blake, R. and Fox, R. (1974). "Binocular rivalry suppression: insensitive to spatial frequency and orientation change." Vision Res. **Aug;14**(8): 687-92.

Blake, R. and Levinson, E. (1977). "Spatial properties of binocular neurones in the human visual system." Exp Brain Res. **Feb 16;27**(2): 221-32.

Blake, R., O'Shea, R. and Mueller, T. (1992). "Spatial zones of binocular rivalry in central and peripheral vision." Vis Neurosci. **8**(5): 469-78.

Blake, R., Sloane, M. and Fox, R. (1981). "Further developments in binocular summation." Percept Psychophys **30**(3): 266-76.

Blake, R., Westendorf, D. and Overton, R. (1980). "What is suppressed during binocular rivalry?" Perception. **9**(2): 223-31.

Blake, R., Yu, K., Lokey, M. and Norman, H. (1998). "Binocular rivalry and motion perception." J Cogn Neurosci. **Jan;10**(1): 46-60.

Bland, J. and Altman, D. (1986). "Statistical methods for assessing agreement between two methods of clinical measurement." Lancet **8**(1): 307-10.

Bowers, A. R., Lovie-Kitchin, J. E. and Woods, R. L. (2001). "Eye movements and reading with large print and optical magnifiers in macular disease." Optom Vis Sci **78**(5): 325-34.

Bowers, A. R. and Reid, V. M. (1997). "Eye movements and reading with simulated visual impairment." Ophthalmic Physiol Opt **17**(5): 392-402.

Brabyn, J., Schneck, M. and Haegerstrom-Portnoy, G. (2001). "The Smith-Kettlewell Institute (SKI) Longitudinal Study of Vision Function and its Impact among the Elderly: an Overview." Optom Vis Sci **2001**: 264-269.
Bressler, N. M. (2000). "Age related macular degeneration. New hope for a common problem comes from photodynamic therapy." Bmj **321**(7274): 1425-7.
Bressler, S., Maguire, M., Bressler, N., al., e. and Group., T. M. P. S. (1990). "Relationship of drusen and abnormalities of the retinal pigment epithelium to the prognosis of neovascular macular degeneration." Arch Ophthalmol **108**: 1442-1447.
Brody, B. L., Gamst, A. C., Williams, R. A., Smith, A. R., Lau, P. W., Dolnak, D., Rapaport, M. H., Kaplan, R. M. and Brown, S. I. (2001). "Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration." Ophthalmology **108**(10): 1893-900; discussion 1900-1.
Brown, B., Yap, M. K. H. and Fan, W. C. S. (1993). "Decrease in stereoacuity in the seventh decade of life." Ophthal Physiol Opt **13**: 138-141.
Brown, B., Zadnik, K., Bailey, I. L. and Colenbrander, A. (1984). "Effect of luminance, contrast, and eccentricity on visual acuity in senile macular degeneration." Am J Optom Physiol Opt **61**(4): 265-70.
Bullimore, M. A. and Bailey, I. L. (1995). "Reading and eye movements in age related maculopathy." Optom Vis Sci **72**: 125-138.
Bullimore, M. A., Bailey, I. L. and Wacker, R. T. (1991). "Face recognition in age-related maculopathy." Invest Ophthalmol Vis Sci **32**: 2020-2029.
Cacho, I., Dickinson, C. M., Smith, H. J. and Harper, R. J. (2003). Fixation characteristics and visual acuity in people with AMD. United Kingdom Multidisciplinary Low Vision Rehabilitation and Research Conference, Birmingham, UK.
Cagenello, R., Arditi, A. and Halpern, D. L. (1993). "Binocular enhancement of visual acuity." J Opt Soc Am A **10**(8): 1841-8.
Campbell, F. W. and Green, D. G. (1965). "Monocular versus binocular visual acuity." Nature **208**(6): 191-2.
Campos, E. C. (1980). "Anomalous retinal correspondence. Monocular and binocular visual evoked responses." Arch Ophthalmol **98**(2): 299-302.
Carbajal, U. (1957). "Plotting the blindspot." Am J Ophthalmol. **44**(3): 379-84.
Casten, R. J., Rovner, B. W. and Tasman, W. (2004). "Age-related macular degeneration and depression: a review of recent research." Curr Opin Ophthalmol **15**(3): 181-3.
Challa, J., Gillies, M., Penfold, P., Gyory, J., Hunyor, A. and Billson, F. (1998). "Exudative macular degeneration and intravitreal triamcinolone: 18 month follow up." Aust N Z J Ophthalmol **26**(4): 277-81.
Chamlin, M. (1960). "Fluctuations in size of the normal blind spot." Arch Ophthalmol. **64**(Oct): 522-7.
Chen, X. and He, S. (2003). "Temporal characteristics of binocular rivalry: visual field asymmetries." Vision Res. **Sep;43**(21): 2207-12.
Chong, N. H. and Bird, A. C. (1998). "Alternative therapies in exudative age related macular degeneration." Br J Ophthalmol **82**(12): 1441-3.
Chuang, E. and Bird, A. (1988). "Bilaterality of tears of the retinal pigment epithelium." Br J Ophthalmol.(72): 918-920.
Ciulla, T. A., Harris, A., Kagemann, L., Danis, R. P., Maturi, R., McNulty, L., Pratt, L. M., Xiao, M., Criswell, M. H. and Weinberger, D. (2001). "Transpupillary thermotherapy for subfoveal occult choroidal

neovascularization: effect on ocular perfusion." Invest Ophthalmol Vis Sci 42(13): 3337-40.
Cobb, W. A., Ettlinger, G. and Morton, H. B. (1967). "Visual potentials evoked in binocular rivalry." Electroencephalogr Clin Neurophysiol 23(4): 397-8.
Cogan, A. (1987). "Human binocular interaction: towards a neural model." Vision Res. 27(12): 2125-39.
Collins, J. K. (1987). "Coping with the rising incidence of partial sight." Optometry Today 27: 772-779.
Crawford, M. and Cool, S. (1970). "Binocular stimulation and response variability of striate cortex units in the cat." Vision Res. Nov;10(11): 1145-53.
Crossland, M. D. and Rubin, G. S. (2002). "The use of an infrared eyetracker to measure fixation stability." Optom Vis Sci 79(11): 735-9.
Crossland, M. D., Sims, M., Galbraith, R. F. and Rubin, G. S. (2004a). "Evaluation of a new quantitative technique to assess the number and extent of preferred retinal loci in macular disease." Vision Res 44(13): 1537-46.
Crossland, M. D., Culham, L. E. and Rubin, G. S. (2004b). "Fixation stability and reading speed in patients with newly developed macular disease*." Ophthalmic Physiol Opt 24(4): 327-33.
Crossland, M. D., Culham, L. E., Kabanarou, S. A. and Rubin, G. S. (2004c). "The development of the preferred retinal locus in patients with macular disease: a longitudinal study." Ophthalmology in press.
Crossland, M. D. (2004d). The development of optimal viewing strategies in people with macular disease. Vision Rehabilitation department, Institute of Ophthalmology, University College of London.
Culham, L., Fitzke, F. and Marshall, J. (1997). "Training of patients with age-related macular disease (AMD) using a scanning laser ophthalmoscope (SLO)." Ophthal Physiol Opt 17(6): 542.
Culham, L., Fitzke, F. W., Timberlake, G. T. and Marshall, J. (1992). "Use of scrolled text in a scanning laser ophthalmoscope to assess reading performance at different retinal locations." Opthalmic Physiol Opt 12: 281-286.
Culham, L., Fitzke, F. W., Timberlake, G. T. and Marshall, J. (1993). "Assessment of fixation stability in normal subjects and patients using a scanning laser ophthalmoscope." Clin Vision Sci 8: 551-561.
Culham, L. E., Ryan, B., Jackson, A. J., Hill, A. R., Jones, B., Miles, C., Young, J. A., Bunce, C. and Bird, A. C. (2002). "Low vision services for vision rehabilitation in the United Kingdom." Br J Ophthalmol 86(7): 743-7.
Cummings, R. W., Whittaker, S. G., Watson, G. R. and Budd, J. M. (1985). "Scanning characters and reading with a central scotoma." Am J Optom Physiol Opt 62: 833-843.
Curcio, C., Owsley, C. and Jackson, G. (2000). "Spare the rods, save the cones in aging and age-related maculopathy." Invest Ophthalmol Vis Sci. Jul;41(8): 2015-8.
Curcio, C. A. and Millican, C. L. (1999). "Basal linear deposit and large drusen are specific for early age-related maculopathy." Arch Ophthalmol 117(3): 329-39.
D'Amato, R., Loughnan, M., Flynn, E. and Folkman, J. (1994). "Thalidomide is an inhibitor of angiogenesis." Proc Natl Acad Sci U S A 91(9): 4082-5.
D'Amico, D., Goldberg, M., Hudson, H., Jerdan, J., Krueger, S., Luna, S., Robertson, S., Russell, S., Singerman, L., Slakter, J., Sullivan, E.,

Yannuzzi, L. and Zilliox, P. (2003). "Anecortave Acetate Clinical Study Group. Anecortave acetate as monotherapy for the treatment of subfoveal lesions in patients with exudative age-related macular degeneration (AMD): interim (month 6) analysis of clinical safety and efficacy." Retina(23): 14-23.

de Belsunce, S. and Sireteanu, R. (1991). "The time course of interocular suppression in normal and amblyopic subjects." Invest Ophthalmol Vis Sci 32(9): 2645-52.

de Juan, E., Jr., Loewenstein, A., Bressler, N. M. and Alexander, J. (1998). "Translocation of the retina for management of subfoveal choroidal neovascularization II: a preliminary report in humans." Am J Ophthalmol 125(5): 635-46.

Deruaz, A., Matter, M., Whatham, A. R., Goldschmidt, M., Duret, F., Issenhuth, M. and Safran, A. B. (2004). "Can fixation instability improve text perception during eccentric fixation in patients with central scotomas?" Br J Ophthalmol 88(4): 461-3.

Deruaz, A., Whatham, A. R., Mermoud, C. and Safran, A. B. (2002). "Reading with multiple preferred retinal loci: implications for training a more efficient reading strategy." Vision Res 42(27): 2947-57.

Desmettre, T., Maurage, C. A. and Mordon, S. (2001). "Heat shock protein hyperexpression on chorioretinal layers after transpupillary thermotherapy." Invest Ophthalmol Vis Sci 42(12): 2976-80.

Dickinson, C. (1998). Low vision: Principles and Practice. Butterworth-Heinemann.

Dithmar, S., Bellmann, C., Holz, F. G. and Volcker, H. E. (1997). "[Confocal scanning laser indocyanine green angiography of classical choroid neovascularization]." Ophthalmologe 94(5): 343-7.

Donzis, P. B., Rappazzo, J. A., Burde, R. M. and Gordon, M. (1983). "Effect of binocular variations of Snellen's visual acuity on Titmus stereoacuity." Arch Ophthalmol 101(6): 930-2.

Duke-Elder, S. (1939). Text-book of Ophthalmology. St Louis. The C.V. Mosby Company. Vol. 1.

Duret, F., Issenhuth, M. and Safran, A. (1999). "Combined use of several preferred retinal loci in patients with macular disorders when reading single words." Vis Re 39: 873-879.

Eames, T. H. and Cambridge, M. (1933). "Physiological Exophoria in relation to Age." Arch Ophthalmol 9: 104-105.

Eckardt, C., Eckardt, U. and Conrad, H. (1999). "Macular rotation with and without counter-rotation of the globe in patients with age-related macular degeneration." Graefes Arch Clin Exp Ophthalmol 237(4): 313-25.

Elliott, D. B., Bullimore, M. A. and Bailey, I. L. (1991). "Improving the reliability of the Pelli-Robson contrast sensitivity test." Clin Vision Sci 6: 471-475.

Elliott, D. B. and Sheridan, M. (1988). "The use of accurate visual acuity measurements in clinical anti-cataract formulation trials." Ophthalmic Physiol Opt 8(4): 397-401.

Elliott, D. B., Trukolo-Ilic, M., Strong, J. G., Pace, R., Plotkin, A. and Bevers, P. (1997). "Demographic characteristics of the vision-disabled elderly." Invest Ophthalmol Vis Sci 38(12): 2566-75.

Ergun, E., Maar, N., Radner, W., Barbazetto, I., Schmidt-Erfurth, U. and Stur, M. (2003). "Scotoma size and reading speed in patients with subfoveal occult choroidal neovascularization in age-related macular degeneration." Ophthalmology 110(1): 65-9.

Erkelens, C. and Collewijn, H. (1985). "Eye movements and stereopsis during dichoptic viewing of moving random-dot stereograms." Vision Res. 25(11): 1689-700.
Evans, J. (2001). "Risk factors for age-related macular degeneration." Prog Retin Eye Res 20: 227-53.
Evans, J., Rooney, C., Ashwood, F., Dattani, N. and Wormald, R. (1996). "Blindness and partial sight in England and Wales: April 1990-March 1991." Health Trends 28: 5-12.
Eyetech Study Group. (2002). "Preclinical and phase 1A clinical evaluation of an anti-VEGF pegylated aptamer (EYE001) for the treatment of exudative age-related macular degeneration." Retina 22(2): 143-52.
Eyetech Study Group. (2003). "Anti-vascular endothelial growth factor therapy for subfoveal choroidal neovascularization secondary to age-related macular degeneration: phase II study results." Ophthalmology 110(5): 979-86.
Evans, J. and Wormald, R. (1996). "Is the incidence of registrable age-related macular degeneration increasing?" Br J Ophthalmol 80(1): 9-14.
Faubert, J. and Overbury, O. (2000). "Binocular vision in older people with adventitious visual impairment: sometimes one eye is better than two." J Am Geriatr Soc 48(4): 375-80.
Ferris, F. L., Kassoff, A., Bresnick, G. H. and Bailey, I. (1982). "New visual acuity charts for clinical research." Am J Ophthalmol 94: 91-96.
Fine, E. M. and Rubin, G. S. (1999a). "Reading with simulated scotomas: attending to the right is better than attending to the left." Vision Res 39(5): 1039-48.
Fine, E. M. and Rubin, G. S. (1999b). "Reading with central field loss: number of letters masked is more important than the size of the mask in degrees." Vision Res 39(4): 747-56.
Finger, P. T., Berson, A., Sherr, D., Riley, R., Balkin, R. A. and Bosworth, J. L. (1996). "Radiation therapy for subretinal neovascularization." Ophthalmology 103(6): 878-89.
Fletcher, D. C. and Schuchard, R. A. (1997). "Preferred retinal loci relationship to macular scotomas in a low-vision population." Ophthalmology 104(4): 632-8.
Fletcher, D. C., Schuchard, R. A. and Watson, G. (1999). "Relative locations of macular scotomas near the PRL: effect on low vision reading." J Rehabil Res Dev 36(4): 356-64.
Forster, K. I. (1970). "Visual perception of rapidly presented words of varying complexity." Percept Psych. 8: 215-221.
Fosse, P., Valberg, A. and Arnljot, H. (2001). "Retinal illuminance and the dissociation of letter and grating acuity in age-related macular degeneration." Optom Vis Sci. Mar;78(3): 162-8.
Fox, R. and Check, R. (1972). "Independence between binocular rivalry suppression duration and magnitude of suppression." J Exp Psychol 93(2): 283-9.
Friedman, J. R., Kosmorsky, G. S. and Burde, R. M. (1985). "Stereoacuity in patients with optic nerve disease." Arch Ophthalmol 103(1): 37-8.
Frisby, J. P., Mein, J., Saye, A. and Stanworth, A. (1975). "Use of random-dot sterograms in the clinical assessment of strabismic patients." Br J Ophthalmol 59(10): 545-52.
Garway-Heath, D. F. and Hitchings, R. A. (1999). "Measurement of optic disc size." Br J Ophthalmol 83(2): 252.

Garway-Heath, D. F., Rudnicka, A. R., Lowe, T., Foster, P. J., Fitzke, F. W. and Hitchings, R. A. (1998). "Measurement of optic disc size: equivalence of methods to correct for ocular magnification." Br J Ophthalmol. 82(6): 643-9.

Gass, J. D. (1994). "Biomicroscopic and histopathologic considerations regarding the feasibility of surgical excision of subfoveal neovascular membranes." Am J Ophthalmol 118(3): 285-98.

Gilchrist, J. and McIver, C. (1985). "Fechner's paradox in binocular contrast sensitivity." Vision Res 25(4): 609-13.

Gilchrist, J. and Pardhan, S. (1987). "Binocular contrast detection with unequal monocular illuminance." Ophthalmic Physiol Opt. 7(4): 373-7.

Gillies, M., Simpson, J., Luo, W., Penfold, P., Hunyor, A., Chua, W., Mitchell, P. and Billson, F. (2003). "A randomized clinical trial of a single dose of intravitreal triamcinolone acetonide for neovascular age-related macular degeneration: one-year results." Arch Ophthalmol 121: 667-73.

Goodrich, G. L., Overbury, O., Mehr, E. B. and Harsh, M. (1985). "A low vision training manual- the VETBook." Invest Ophthalmol 26: 219.

Green, W., McDonnell, P. and Yeo, J. (1985). "Pathologic features of senile macular degeneration." Ophthalmology 92: 615-627.

Gregor, Z., Bird, A. and Chisholm, I. (1977). "Senile disciform macular degeneration in the second eye." Br J Ophthalmol. 61: 141-147.

Grigsby, S. and Tsou, B. (1994). "Grating and flicker sensitivity in the near and far periphery: naso-temporal asymmetries and binocular summation." Vision Res. Nov;34(21): 2841-8.

Grizzard, S., Arnett, D. and Haag, S. (2003). "Twin study of age-related macular degeneration." Ophthalmic Epidemiol 10: 315-22.

Group., P. T. f. M. D. S. (1997). "Interferon alfa-2a is ineffective for patients with choroidal neovascularization secondary to age-related macular degeneration. Results of a prospective randomized placebo-controlled clinical trial." Arch Ophthalmol 115(7): 865-72.

Guez, J.-E., Le Gargasson, J.-F., Rigaudiere, F. and O'Regan, J. K. (1993). "Is there a systematic location for the pseudo-fovea in patients with central scotoma?" Vision Res 33: 1271-1279.

Haegerstrom-Portnoy, G., Schneck, M. and Brabyn, J. A. (1999). "Seeing into old age: visual function beyond acuity." Optom Vis Sci 76: 141-58.

Hall, C. (1982). "The relationship between clinical stereotests." Ophthalmic Physiol Opt 2(2): 135-43.

Hammond, B. R., Jr. and Caruso-Avery, M. (2000). "Macular pigment optical density in a Southwestern sample." Invest Ophthalmol Vis Sci 41(6): 1492-7.

Hammond, C., Webster, A., Snieder, H., Bird, A., Gilbert, C. and Spector, T. (2002). "Genetic influence on early age-related maculopathy: a twin study." Ophthalmology 109: 730-6.

Harrad, R., Sengpiel, F. and Blakemore, C. (1996). "Physiology of suppression in strabismic amblyopia." Br J Ophthalmol 80(4): 373-7.

Hazel, C. A., Petre, K. L., Armstrong, R. A., Benson, M. T. and Frost, N. A. (2000). "Visual function and subjective quality of life compared in subjects with acquired macular disease." Invest Ophthalmol Vis Sci 41(6): 1309-15.

Hirsch, M. J. and Weymouth, F. W. (1948). "Distance discrimination." Arch Ophthalmol 39: 210-223.

Holcomb, J. G. and Goodrich, G. L. (1976). "Eccentric viewing training." J Am

Optom Assoc 47: 1438-1443.
Holz, F. G., Bellmann, C., Rohrschneider, K., Burk, R. O. and Volcker, H. E. (1998). "Simultaneous confocal scanning laser fluorescein and indocyanine green angiography." Am J Ophthalmol 125(2): 227-36.
Holz, F. G., Pauleikhoff, D., Spaide, R. F. and Bird, A. C. (2003). Age-related macular degeneration. Springer-Verlag Berlin Heidelberg.
Home, R. (1978). "Binocular summation: A study of contrast sensitivity, visual acuity and recognition." Vision Res 18: 579-585.
Hooper, C. Y. and Guymer, R. H. (2003). "New treatments in age-related macular degeneration." Clin Experiment Ophthalmol 31(5): 376-91.
Horowitz, A. (1994). "Vision impairment and functional disability among nursing home residents." Gerontologist 34(3): 316-23.
Hu, S., Schuchard, R., Fletcher, D. and Sabates, F. (1994). Physiological blind spot characteristics and position relative to retinal locus for fixation by SLO testing. Invest Ophthal Vis Sci 35 Abstract S1527.
Hyson, M., Julesz, B. and Fender, D. (1983). "Eye movements and neural remapping during fusion of misaligned random-dot stereograms." J Opt Soc Am. Dec;73(12): 1665-73.
Jacobs, R. J. (1979). "Visual resolution and contour interaction in the fovea and periphery." Vision Res 19(11): 1187-95.
Jenkins, T. C., Abd-Manan, F., Pardhan, S. and Murgatroyd, R. N. (1994). "Effect of fixation disparity on distance binocular visual acuity." Ophthalmic Physiol Opt 14(2): 129-31.
Jonas, J. (2005). "Optic disk size correlated with refractive error." Am J Ophthalmol 139(2): 346-348.
Kawasaki, K., Hirose, T., Jacobson, J. H. and Cordella, M. (1970). "Binocular fusion. Effect of breaking on the human visual evoked response." Arch Ophthalmol 84(1): 25-8.
Klein, R., Klein, B. and Linton, K. (1992). "Prevalence of age-related maculopathy. The Beaver Dam Eye Study." Ophthalmology 99: 933-943.
Klein, R., Klein, B. E., Linton, K. L. and De Mets, D. L. (1991). "The Beaver Dam Eye Study: visual acuity." Ophthalmology 98(8): 1310-5.
Kosnik, W., Fikre, J. and Sekuler, R. (1986). "Visual fixation stability in older adults." Invest Ophthalmol Vis Sci 27(12): 1720-5.
Kovacs, I., Papathomas, T., Yang, M. and Feher, A. (1996). "When the brain changes its mind: interocular grouping during binocular rivalry." Proc. Natl. Acad. Sci. USA 93: pp. 15508-15511.
Krieger, A. A. (1967). "The partially sighted patient: a study of 917 cases." Trans Am Ophthalmol Soc 65: 544-90.
Lam, A. K., Chau, A. S., Lam, W. Y., Leung, G. Y. and Man, B. S. (1996). "Effect of naturally occurring visual acuity differences between two eyes in stereoacuity." Ophthalmic Physiol Opt 16(3): 189-95.
Lappas, A., Weinberger, A. W., Foerster, A. M., Kube, T., Rezai, K. A. and Kirchhof, B. (2000). "Iris pigment epithelial cell translocation in exudative age-related macular degeneration. A pilot study in patients." Graefes Arch Clin Exp Ophthalmol 238(8): 631-41.
Larson, W. L. and Bolduc, M. (1991). "Effect of induced blur on visual acuity and stereoacuity." Optom Vis Sci 68(4): 294-8.
Lavin, M., Eldem, B. and Gregor, Z. (1991). "Symmetry of disciform scars in bilateral age-related macular degeneration." Br J Ophthalmol. 75: 133-136.
Lawwill, T. and Biersdorf, W. R. (1968). "Binocular rivalry and visual evoked

responses." Invest Ophthalmol 7(4): 378-85.
Lee, S. and Blake, R. (1999). "Rival ideas about binocular rivalry." Vision Res. Apr;39(8): 1447-54.
Legge, G. and Rubin, G. (1981). "Binocular interactions in suprathreshold contrast perception." Percept Psychophys. Jul;30(1): 49-61.
Legge, G. E. (1984). "Binocular contrast summation--II. Quadratic summation." Vision Res 24(4): 385-94.
Legge, G. E., Ahn, S. J., Klitz, T. S. and Luebker, A. (1997). "Psychophysics of reading-XVI. The visual span in normal and low vision." Vision Res 37: 1999-2010.
Legge, G. E. and Gu, Y. (1989). "Stereopsis and contrast." Vision Res 29: 989-1004.
Legge, G. E., Parish, D. H., Luebker, A. and Wurm, L. H. (1990). "Psychophysics of reading. XI. Comparing color contrast and luminance contrast." J Opt Soc Am A 7(10): 2002-10.
Legge, G. E., Pelli, D. G., Rubin, G. S. and Schleske, M. M. (1985a). "Psychophysics of reading. I. Normal vision." Vision Res 25: 239-252.
Legge, G. E., Ross, J. A., Isenberg, L. M. and LaMay, J. M. (1992). "Psychophysics of reading. Clinical predictors of low-vision reading speed." Invest Ophthalmol Vis Sci 33(3): 677-87.
Legge, G. E., Ross, J. A., Luebker, A. and LaMay, J. M. (1989). "Psychophysics of reading. VIII. The Minnesota Low-Vision Reading Test." Optom Vis Sci 66(12): 843-53.
Legge, G. E. and Rubin, G. S. (1986). "Contrast sensitivity function as a screening test: a critique." Am J Optom Physiol Opt 63(4): 265-70.
Legge, G. E., Rubin, G. S. and Luebker, A. (1987). "Psychophysics of reading--V. The role of contrast in normal vision." Vision Res 27(7): 1165-77.
Legge, G. E., Rubin, G. S., Pelli, D. G. and Schleske, M. M. (1985b). "Psychophysics of reading. II. Low vision." Vision Res 25: 253-266.
Lehky, S. R. (1983). "A model of binocular brightness and binaural loudness perception in humans with general applications to nonlinear summation of sensory inputs." Biol Cybern 49(2): 89-97.
Lei, H. and Schuchard, R. A. (1997). "Using two preferred retinal loci for different lighting conditions in patients with central scotomas." Invest Ophthalmol Vis Sci 38: 1812-1818.
Leonards, U. and Sireteanu, R. (1993). "Interocular suppression in normal and amblyopic subjects: the effect of unilateral attenuation with neutral density filters." Percept Psychophys. Jul;54(1): 65-74.
Leopold, D. and Logothetis, N. (1996). "Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry." Nature Feb 8;379(6565): 549-53.
Levy, N. S. and Glick, E. B. (1974). "Stereoscopic perception and Snellen visual acuity." Am J Ophthalmol 78(4): 722-4.
Lewis, H., Kaiser, P. K., Lewis, S. and Estafanous, M. (1999). "Macular translocation for subfoveal choroidal neovascularization in age-related macular degeneration: a prospective study." Am J Ophthalmol 128(2): 135-46.
Li, C. and Creutzfeldt, O. (1984). "The representation of contrast and other stimulus parameters by single neurons in area 17 of the cat." Pflugers Arch. Jul;401(3): 304-14.
Logothetis, N., Leopold, D. and Sheinberg, D. (1996). "What is rivalling during binocular rivalry?" Nature. Apr 18;380(6575): 621-4.

Lovie-Kitchin, J. E. (1988). "Validity and reliability of visual acuity measurements." Ophthalmic Physiol Opt **8**(4): 363-70.
Lovie-Kitchin, J. E., Bowers, A. R. and Woods, R. L. (2000). "Oral and silent reading performance with macular degeneration." Ophthalmic Physiol Opt **20**(5): 360-70.
Ludvigh, E. (1941). "Extrafoveal visual acuity as measured with Snellen testletters." Arch Ophthalmol.
Lund, R. D., Adamson, P., Sauve, Y., Keegan, D. J., Girman, S. V., Wang, S., Winton, H., Kanuga, N., Kwan, A. S., Beauchene, L., Zerbib, A., Hetherington, L., Couraud, P. O., Coffey, P. and Greenwood, J. (2001). "Subretinal transplantation of genetically modified human cell lines attenuates loss of visual function in dystrophic rats." Proc Natl Acad Sci U S A **98**(17): 9942-7.
Machemer, R. and Steinhorst, U. (1993). "Retinal separation, retinotomy, and macular relocation: II. A surgical approach for age-related macular degeneration?" Graefes Arch Clin Exp Ophthalmol **231**(11): 635-41.
Mackeben, M. and Gofen, A. (2001). The physiological blind spot as a marker for eccentric viewing. Invest Ophthal Vis Sci 42 ARVO Abstract 853.
Macular Photocoagulation Study Group (M. P. S). (1991a). "Argon laser photocoagulation for neovascular maculopathy. Five-year results from randomized clinical trials. " Arch Ophthalmol **109**(8): 1109-14.
Macular Photocoagulation Study Group (M. P. S). (1991b). "Laser photocoagulation of subfoveal recurrent neovascular lesions in agerelated macular degeneration: results of randomized clinical trial." Arch Ophthalmol **109**: 1232-41.
Macular Photocoagulation Study Group (M. P. S). (1993a). "Five-year follow-up of fellow eyes of patients with age-related macular degeneration and unilateral extrafoveal choroidal neovascularization." Arch Ophthalmol **111**: 1189-1199.
Macular Photocoagulation Study Group (M. P. S). (1993b). "Laser photocoagulation of subfoveal neovascular lesions of age-related macular degeneration:update findings from two clinical trials." Arch Ophthalmol **111**: 1200-9.
Maguire, P. and Vine, A. (1986). "Geographic atrophy of the retinal pigment epithelium." Am J Ophthalmol. **102**: 621-625.
Mainster, M. A. and Reichel, E. (2000). "Transpupillary thermotherapy for age relatedmacular degeneration: long-pulse photocoagulation, apoptosis, and heat shock proteins." Ophthalmic Surg Lasers **31**(5): 359-73.
Majji, A. B. and de Juan, E., Jr. (2000). "Retinal pigment epithelial autotransplantation: morphological changes in retina and choroid." Graefes Arch Clin Exp Ophthalmol **238**(9): 779-91.
Mangione, C., Gutierrez, P., Lowe, G., Orav, E. and Seddon, J. (1999). "Influence of age-related maculopathy on visual functioning and healthrelated quality of life." Am J Ophthalmol. **Jul;128**(1): 45-53.
Mangione, C. M., Berry, S., Spritzer, K., Janz, N. K., Klein, R., Owsley, C. and Lee, P. P. (1998). "Identifying the content area for the 51-item National Eye Institute Visual Function Questionnaire: results from focus groups with visually impaired persons." Arch Ophthalmol **116**(2): 227-33.
Margrain, T. H. (2000). "Helping blind and partially sighted people to read: the effectiveness of low vision aids." Br J Ophthalmol **84**(8): 919-21.

Massof, R. W. (2003). Relation of Reading Performance to Visual Acuity and Perceived Reading Ability in Low Vision. Invest Ophthal Vis Sci ARVO Abstract 1284/B180.

McConkie, G. W., Kerr, P. W., Reddix, M. D. and Zola, D. (1988). "Eye movement control during reading: I. The location of initial eye fixations on words." Vision Res **28**(10): 1107-18.

McConkie, G. W., Rayner, K. (1975). "The span of the effective stimulus during a fixation in reading." Perception & Psychophysics **1975**(17): 578-586.

McKee, S. P., Welch, L., Taylor, D. G. and Bowne, S. F. (1990). "Finding the common bond: stereoacuity and the other hyperacuities." Vision Res **30**: 879-891.

McMahon, T. T., Hansen, M., Stelmack, J., Oliver, P. and Viana, M. A. (1993). "Saccadic eye movements as a measure of the effect of low vision rehabilitation on reading rate." Optom Vis Sci **70**(6): 506-10.

McMahon, T. T., Hansen, M. and Viana, M. (1991). "Fixation characteristics in macular disease. Relationship between saccadic frequency, sequencing, and reading rate." Invest Ophthalmol Vis Sci **32**(3): 567-74.

Mehdorn, E. and Kommerell, G. (1978). "'Rebound-saccade' in the prism cover test." Int Ophthalmol **1**(1): 63-6.

Meyer, T. and Howland, H. C. (2001). "How large is the optic disc? Systematic errors in fundus cameras and topographers." Ophthalmic and Physiological Optics **21**(2): 139-150.

Millidot, M. Dictionary of Optometry. 3rd edition. Butterworth Heinemann.

Mireskandari, K., Garnham, L., Sheard, R., Ezra, E., Gregor, Z. J. and Sloper, J. J. (2004). "A prospective study of the effect of a unilateral macular hole on sensory and motor binocular function and recovery following successful surgery." Br J Ophthalmol **88**(10): 1320-4.

Morrison, R. E. and Rayner, K. (1981). "Saccade size in reading depends upon character spaces and not visual angle." Percept Psychophys **30**(4): 395-6.

Nachmias, J. (1959). "Two-dimensional motion of the retinal image during monocular fixation." J Opt Soc Am **49**: 901-8.

Nachmias, J. and Kocher, E. C. (1970). "Visual detection and discrimination of luminance increments." J Opt Soc Am **60**(3): 382-9.

Newsom, R., McAlister, J., Saeed, M. and McHugh, J. (2001). "Transpupillary thermotherapy (TTT) for the treatment of choroidal neovascularisation." Br J Ophthalmol **85**(2): 173-8.

Nilsson, U. L., Frennesson, C. and Nilsson, S. E. (1998). "Location and stability of a newly established eccentric retinal locus suitable for reading, achieved through training of patients with a dense central scotoma." Optom Vis Sci **75**(12): 873-8.

Nilsson, U. L., Frennesson, C. and Nilsson, S. E. (2003). "Patients with AMD and a large absolute central scotoma can be trained successfully to use eccentric viewing, as demonstrated in a scanning laser ophthalmoscope." Vision Res **43**(16): 1777-87.

Nygaard, R. W. and Schuchard, R. A. (2001). "SLO radiant power and brightness." J Rehabil Res Dev **38**(1): 123-8.

Ohzawa, I. and Freeman, R. (1986). "The binocular organization of simple cells in the cat's visual cortex." J Neurophysiol. **Jul;56**(1): 221-42.

Ooi, T. and Loop, M. (1994). "Visual suppression and its effect upon color and luminance sensitivity." Vision Res. **Nov;34**(22): 2997-3003.

Oosterhuis, J. A., Journee-de Korver, H. G., Kakebeeke-Kemme, H. M. and Bleeker, J. C. (1995). "Transpupillary thermotherapy in choroidal melanomas." Arch Ophthalmol 113(3): 315-21.
O'Regan, J. K. (1990). "Eye movements and reading." Rev Oculomot Res 4: 395-453.
Owens, S. L., Guymer, R. H., Gross-Jendroska, M. and Bird, A. C. (1999). "Fluorescein angiographic abnormalities after prophylactic macular photocoagulation for high-risk age-related maculopathy." Am J Ophthalmol 127(6): 681-7.
Owsley, C., Jackson, G., Cideciyan, A., Huang, Y., Fine, S., Ho, A., Maguire, M., Lolley, V. and Jacobson, S. (2000). "Psychophysical evidence for rod vulnerability in age-related macular degeneration." Invest Ophthalmol Vis Sci. Jan;41(1): 267-73.
Owsley, C. and Sloane, M. E. (1987). "Contrast sensitivity, acuity, and the perception of 'real-world' targets." Br J Ophthalmol 71: 791-796.
Pardhan, S. (1993). "Binocular performance in patients with unilateral cataract using the Regan test: binocular summation and inhibition with lowcontrast
charts." Eye 7(1): 59-62.
Pardhan, S. (1996). "A comparison of binocular summation in young and older patients." Curr Eye Res. 15(3): 315-319.
Pardhan, S. (1997). "A comparison of binocular summation in the peripheral visual field in young and older patients." Curr Eye Res 16(3): 252-5.
Pardhan, S. (2003). "Binocular recognition summation in the peripheral visual field: contrast and orientation dependence." Vision Res 43(11): 1249-55.
Pardhan, S. and Gilchrist, J. (1990). "The effect of monocular defocus on binocular contrast sensitivity." Ophthalmic Physiol Opt. Jan;10(1): 33-6.
Pardhan, S. and Gilchrist, J. (1991). "The importance of measuring binocular contrast sensitivity in unilateral cataract." Eye 5(1): 31-5.
Pardhan, S. and Gilchrist, J. (1992). "Binocular contrast summation and inhibition in amblyopia. The influence of the interocular difference on binocular contrast sensitivity." Doc Ophthalmol. 82(3): 239-48.
Pardhan, S. and Whitaker, A. (2003). "Binocular summation to gratings in the peripheral field in older subjects is spatial frequency dependent." Curr Eye Res 26(5): 297-302.
Peli, E. (1986). "Control of eye movement with peripheral vision: implications for training of eccentric viewing." Am J. Opt. & Physiol Optics 63(2): 113-118.
Pelli, D. G., Robson, J. G. and Wilkins, A. J. (1988). "The design of a new letter chart for measuring contrast sensitivity." Clin. Vision Sci. 2: 187-199.
Petre, K. L., Hazel, C. A., Fine, E. M. and Rubin, G. S. (2000). "Reading with eccentric fixation is faster in inferior visual field than in left visual field." Optom Vis Sci 77(1): 34-9.
Piantanida, T. (1986). "Stereo hysteresis revisited." Vision Res. 26(3): 431-7.
Pirenne, M. (1943). "Binocular and uniocular thresholds in vision." Nature 152: 698-699.
Pharmacological Therapy for Macular Degeneration Study Group. (1997). "Interferon alfa-2a is ineffective for patients with choroidal neovascularization secondary to age-related macular degeneration. Results of a prospective randomized placebo-controlled clinical trial." Arch Ophthalmol 115(7): 865-72.
Pollatsek, A., Bolozky, S., Well, A. D. and Rayner, K. (1981). "Asymmetries in

the perceptual span for Israeli readers." Brain and Language 14: 174-180.
Pollatsek, A., Tan, L. H. and Rayner, K. (2000). "The role of phonological codes in integrating information across saccadic eye movements in Chinese character identification." J Exp Psychol Hum Percept Perform 26(2): 607-33.
Potter, J. and Thaliemer, J. (1981). "Geographic atrophy of the retinal pigment epithelium: diagnosis and vision rehabilitation." J Am Optom Assoc. 52: 503-508.
Pratt-Johnson, J. A. (1988). "Fusion ability lost and regained in visual adults." Graefes Arch Clin Exp Ophthalmol 226(2): 111-2.
Raasch, T. W. (2004). "What we don't know about eccentric viewing. The link between central scotomas, Troxler fading, and preferred retinal locus." Br J Ophthalmol 88: 443.
(RAD) Study Group. (1999). "The Radiation Therapy for Age-related Macular Degeneration. A prospective, randomized, double-masked trial on radiation therapy for neovascular age-related macular degeneration." ophthalmology 106: 2239-47.
Raney, G. E. and Rayner, K. (1995). "Word frequency effects and eye movements during two readings of a text." Can J Exp Psychol 49(2): 151-72.
Rayner, K. (1975). "The perceptual span and peripheral cues in reading." Cog. Psychol. 7: 65-81.
Rayner, K. (1978). "Eye movements in reading and information processing." Psychol Bull 85: 618-660.
Rayner, K. (1979). "Eye guidance in reading: Fixation location within words." Perception 8: 21-30.
Rayner, K. and Bertera, J. H. (1979). "Reading without a fovea." Science 206: 468-469.
Rayner, K., Well, A. D. and Pollatsek, A. (1980). "Asymmetry of the effective visual field in reading." Percept Psychophys 27(6): 537-44.
Rees, A., Kabanarou, S., Culham, L. and Rubin, G. (2004). Does peripheral visual acuity influence PRL location in AMD? Invest Ophthal Vis Sci ARVO Abstract 3066/B701.
Reeves, B. C., Wood, J. M. and Hill, A. R. (1991). "Vistech VCTS 6500 charts--within- and between-session reliability." Optom Vis Sci 68(9): 728-37.
Reichel, E., Berrocal, A. M., Ip, M., Kroll, A. J., Desai, V., Duker, J. S. and Puliafito, C. A. (1999). "Transpupillary thermotherapy of occult subfoveal choroidal neovascularization in patients with age-related macular degeneration." Ophthalmology 106(10): 1908-14.
Richer, S., Stiles, W., Statkute, L., Pei, K., Frankowski, J., Nyland, J., Pulido, J. and Rudy, D. (2002). The Lutein Antioxidant Supplementation Trial. Invest. Ophthalmol. Vis. Sci. ARVO 43: E-Abstract 2542.
Richer, S., Stiles, W., Statkute, L., Pulido, J., Frankowski, J., Rudy, D., Pei, K., Tsipursky, M. and Nyland, J. (2004). "Double-masked, placebocontrolled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial)." Optometry 75(4): 216-30.
Robinson, B., Acorn, C. J., Millar, C. C. and Lyle, W. M. (1997). "The prevalence of selected ocular diseases and conditions." Optom Vis Sci 74(2): 79-91.

Rohrschneider, K., Becker, M., Schumacher, N., Fendrich, T. and Volcker, H. E. (1998). "Normal values for fundus perimetry with the scanning laser ophthalmoscope." Am J Ophthalmol **126**(1): 52-8.
Rohrschneider, K., Fendrich, T., Becker, M., Krastel, H., Kruse, F. E. and Volcker, H. E. (1995). "Static fundus perimetry using the scanning laser ophthalmoscope with an automated threshold strategy." Graefes Arch Clin Exp Ophthalmol **233**(12): 743-9.
Romano, P. E. and von Noorden, G. K. (1971). "Limitations of cover test in detecting strabismus." Am J Ophthalmol **72**(1): 10-2.
Romayananda, N., Wong, S. W., Elzeneiny, I. H. and Chan, G. H. (1982). "Prismatic scanning method for improving visual acuity in patients with low vision." Ophthalmology **89**(8): 937-45.
Rosenberg, R., Faye, E., Fischer, M. and Budick, D. (1989). "Role of prism relocation in improving visual performance of patients with macular dysfunction." Optom Vis Sci **66**: 747-750.
Rovner, B. W. and Casten, R. J. (2002). "Activity loss and depression in age relatedmacular degeneration." Am J Geriatr Psychiatry **10**(3): 305-10.
Rovner, B. W., Casten, R. J. and Tasman, W. S. (2002). "Effect of depression on vision function in age-related macular degeneration." Arch Ophthalmol **120**(8): 1041-4.
Roy, M. and Kaiser Kupfer, M. (1990). "Second eye involvement in age-related macular degeneration: a four-year prospective study." Eye **4**: 813-818.
Rubin, G. S. (2001). "Vision rehabilitation for patients with age-related macular degeneration." Eye **15**(Pt 3): 430-5.
Rubin, G. S., Adamsons, I. A. and Stark, W. J. (1993). "Comparison of acuity, contrast sensitivity, and disability glare before and after cataract surgery." Arch Ophthalmol **111**: 56-61.
Rubin, G. S., Bandeen-Roche, K., Huang, G.-H., Munoz, B., Schein, O. D., Fried, L. P., West, S. K. and for the SEE project team (2001). "The association of multiple visual impairments with eself-reported visual disability: SEE project." Invest Ophthalmol Vis Sci **42**: 64-72.
Rubin, G. S. and Legge, G. E. (1985). Predicting low-vision reading rates from measures of contrast sensitivity. Noninvasive Assessment of the Visual System, Technical Digest Series. Washington., D.C., Optical Society of America**:** 1-10.
Rubin, G. S. and Legge, G. E. (1989). "Psychophysics of reading. VI--The role of contrast in low vision." Vision Res **29**(1): 79-91.
Rubin, G. S., Munoz, B., Bandeen-Roche, K. and West, S. K. (2000). "Monocular versus binocular visual acuity as measures of vision impairment and predictors of visual disability." Invest Ophthalmol Vis Sci **41**(11): 3327-34.
Rubin, G. S. and Turano, K. (1992). "Reading without saccadic eye movements." Vision Res **32**: 895-902.
Rubin, G. S. and Turano, K. (1994). "Low vision reading with sequential word presentation." Vision Res **34**: 1723-1733.
Rubin, G. S., West, S. K., Munoz, B., Bandeen-Roche, K., Zeger, S., Schein, O. and Fried, L. P. (1997). "A comprehensive assessment of visual impairment in a population of older Americans. The SEE Study. Salisbury Eye Evaluation Project." Invest Ophthalmol Vis Sci **38**(3): 557-68.
Rudnicka, A. R., Burk, R. O., Edgar, D. F. and Fitzke, F. W. (1998). "Magnification characteristics of fundus imaging systems."

Ophthalmology 105(12): 2186-92.
Rudnicka, A. R. and Edgar, D. F. (1995). "Automated static perimetry in myopes with peripapillary crescents--Part I." Ophthalmic Physiol Opt 15(5): 409-12.
Sansbury, R. V., Skavenski, A. A., Haddad, G. M. and Steinman, R. M. (1973). "Normal fixation of eccentric targets." J Opt Soc Am 63(5): 612-4.
Sarks, J., Sarks, S. and Killingsworth, M. (1988). "Evolution of geographic atrophy of the retinal pigment epithelium." Eye. 2: 552-577.
Schatz, H. and McDonald, H. (1989). "Atrophic macular degeneration: rate of spread of geographic atrophy and visual loss." Ophthalmology 96: 1541-1551.
Scheider, A., Gundisch, O. and Kampik, A. (1999). "Surgical extraction of subfoveal choroidal new vessels and submacular haemorrhage in agerelated
macular degeneration: results of a prospective study." Graefes Arch Clin Exp Ophthalmol 237(1): 10-5.
Schmidt-Erfurth, U., Hasan, T., Gragoudas, E., Michaud, N., Flotte, T. J. and Birngruber, R. (1994). "Vascular targeting in photodynamic occlusion of subretinal vessels." Ophthalmology 101(12): 1953-61.
Schor, C., Terrell, M. and Peterson, D. (1976). "Contour interaction and temporal masking in strabismus and amblyopia." Am J Optom Physiol Opt. May;53(5): 217-23.
Schuchard, R., Cummings, R., Ross, D. and Watson, G. (2003). "Comparison of SLO Perimetry, Binocular Perimetry, and Functional Visual Field Perimetry in Patients with Macular Scotomas." Invest Ophthal Vis Sci ARVO Abstract 2778/B617.
Schuchard, R. A. (1995). "Adaptation to macular scotomas in persons with low vision." Am J Occup Ther 49(9): 870-6.
Schuchard, R. A. and Fletcher, D. C. (1994). "Preferred retinal locus: A review with applications in low vision rehabilitation." Ophthalmol Clin North Am 7: 243-256.
Schuchard, R. A., Fletcher, D. C. and Maino, J. (1994). "A Scanning Laser Opthalmoscope (SLO) low-vision rehabitiltaion system." Clin. Eye Vision Care 6: 101-107.
Schuchard, R. A. and Raasch, T. W. (1992). "Retinal locus for fixation: Pericentral fixation targets." Clinical Vision Science 7(6): 511-520.
Schuchard, R. A., Tekwani, N. and Hu, S. (1995). Binocular preferred retinal loci: Relationship of visual factors to binocular perception. Vision science and its applications (OSA Technical Digest Series).
Shah, M. B., Fishman, G. A., Alexander, K. R. and Viana, M. (1995). "Stereoacuity testing in patients with retinal and optic nerve disorders." Doc Ophthalmol 91(3): 265-71.
Sheedy, J. E. and Saladin, J. J. (1975). "Exophoria at near in presbyopia." Am J Optom Physiol Opt 52: 474-481.
Sireteanu, R., Fronius, M. and Constantinescu, D. (1994). "The development of visual acuity in the peripheral visual field of human infants: binocular and monocular measurements." Vision Res. Jun;34(12): 1659-71.
Slakter, J. A. A. C. S. G. (2003). "Anecortave acetate as monotherapy for treatment of subfoveal neovascularization in age-related macular degeneration: twelve-month clinical outcomes." Ophthalmology 110: 2372-83.
Smith, E., Levi, D., Harwerth, R. and White, J. (1982). "Color vision is altered

during the suppression phase of binocular rivalry." Science. Nov 19;218(4574): 802-4.
Smith, E. L., 3rd, Levi, D. M., Manny, R. E., Harwerth, R. S. and White, J. M. (1985). "The relationship between binocular rivalry and strabismic suppression." Invest Ophthalmol Vis Sci 26(1): 80-7.
Smith, H. J., Dickinson, C. M., Reeves, B. C., Cacho, I. and Harper, R. A. (2003). Can prism spectacles reduce disability in AMD? United Kingdom Multidisciplinary Low Vision Rehabilitation and Research Conference, Birmingham, UK.
Smith, W. (2001). "Risk factors for age-related macular degeneration: pooled findings from three continents." Ophthalmology 108: 697-704.
Snydacker, D. (1962). "The Maddox rod test: a 10-year follow up." Trans Am Ophthalmol Soc 60: 292-303.
Sperduto, R. and Seigel, D. (1980). "Senile lens and senile macular changes in a population-based sample." Am J Ophthalmol 90: 86-91.
Steinbach, M. J. (1981). "Alternating exotropia: temporal course of the switch in suppression." Invest Ophthalmol Vis Sci 20(1): 129-33.
Steinman, R. M., Cushman, W. B. and Martins, A. J. (1982). "The Precision of Gaze." Human Neurobiol(1): 97-109.
Steinman, S., Steinmann, B. and Garzia, R. (2000). Foundations of binocular vision. A clinical perspective. The McGraw-Hill Companies.
Steinmann, R. (1965). "Effect of target size, luminance, and color on monocular fixation." Journal of the Optical Society of America 55(9): 1158-1165.
Strahlman, E., Fine, S. and Hillis, A. (1983). "The second eye of patients with senile macular degeneration." Arch Ophthalmol 101: 1191-1193.
Sunness, J. S., Applegate, C. A., Haselwood, D. and Rubin, G. S. (1996). "Fixation patterns and reading rates in eyes with central scotomas from advanced atrophic age-related macular degeneration and Stargardt disease." Ophthalmology 103(9): 1458-66.
Sunness, J. S., J., B.-G., Applegate, C. A., Bressler, N. M., Tian, Y., Hawkins, B., Barron, Y. and Bergman, A. (1999). "Enlargement of Atrophy and Visual Acuity, Loss in the Geographic Atrophy Form of Age-related Macular Degeneration." Journal Of Ophthalmology 106(9): 1768-1779.
Sunness, J. S., Schuchard, R. A., Shen, N., Rubin, G., Dagnelie, G. and Haselwood, D. M. (1995). "Landmark-driven fundus perimetry using the scanning laser ophthalmoscope." Invest Ophthalmol Vis Sci 36: 1863-1874.
Sunness J, Applegate CA, Gonzalez-Baron J (2000). Improvement of visual acuity over time in patients with bilateral geographic atrophy from age-related macular degeneration. Retina;20:162-169.
(TAP) Study Group. (1999). "Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of 2 randomized clinical trials--TAP report. Treatment of age-related macular degeneration with photodynamic therapy." Arch Ophthalmol 117(10): 1329-45.
(TAP) Study Group. (2001). "Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials--TAP report 2. Treatment of age-related macular degeneration with photodynamic therapy." Arch Ophthalmol 119: 198-207.
Tejeria, L., Harper, R. A., Artes, P. H. and Dickinson, C. M. (2002). "Face recognition in age related macular degeneration: perceived disability,

measured disability, and performance with a bioptic device." Br J Ophthalmol 86(9): 1019-26.
Tezel, T. H., Del Priore, L. V., Flowers, B. E., Grosof, D. H., Benenson, I. L., Zamora, R. L. and Kaplan, H. J. (1996). "Correlation between scanning laser ophthalmoscope microperimetry and anatomic abnormalities in patients with subfoveal neovascularization." Ophthalmology 103(11): 1829-36.
Thorn, F. and Boynton, R. M. (1974). "Human binocular summation at absolute threshold." Vision Res 14(7): 445-58.
Thumann, G. (2001). "Development and cellular functions of the iris pigment epithelium." Surv Ophthalmol 45(4): 345-54.
Timberlake, G. T., Mainster, M. A., Peli, E., Augliere, R. A., Essock, E. A. and Arend, L. E. (1986). "Reading with a macular scotoma. I. Retinal location of scotoma and fixation area." Invest Ophthalmol Vis Sci 27: 1137-47.
Timberlake, G. T., Pelli, E., Essock, E. A. and Augliere, R. A. (1987). "Reading with a macular scotoma. II. Retinal locus for scanning text." Invest Ophthalmol Vis Sci 28: 1268-1274.
The Choroidal Neovascularisation Prevention Trial Research Group (T. C. N. P. T. R.). (1998a). "Laser treatment in eyes with large drusen. Short term effects seen in a pilot randomized clinical trial." Ophthalmology 105: 11-23.
The Choroidal Neovascularisation Prevention Trial Research Group (T. C. N. P. T. R.). (1998b). "Choroidal neovascularisation in the Choroidal Neovascularisation Prevention Trial." Ophthalmology 105: 1364-1372.
Valberg, A. and Fosse, P. (2002). "Binocular contrast inhibition in subjects with age-related macular degeneration." J Opt Soc Am A Opt Image Sci Vis. Jan;19(1): 223-8.
Valmaggia, C., Ries, G. and Ballinari, P. (2002). "Radiotherapy for subfoveal choroidal neovascularization in age-related macular degeneration: a randomized clinical trial." Am J Ophthalmol 133(4): 521-9.
van den Berg, T. J. (1995). "Analysis of intraocular straylight, especially in relation to age." Optom Vis Sci 72(2): 52-9.
Vingerling, J. R., Dielemans, I., Hofman, A., Grobbee, D. E., Hijmering, M., Kramer, C. F. and de Jong, P. T. (1995). "The prevalence of age-related maculopathy in the Rotterdam Study." Ophthalmology 102(2): 205-10.
(VIP) Study Group. (2001). "Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularisation-- Verteporfin in photodynamic therapy report 2.." Am J Ophthalmol 131: 541-60.
von Noorden, G. and Campos, E. (2002). Binocular vision and ocular motility. Theory and management of strabismus. Mosby.
von Noorden, G. and Mackensen, G. (1962). "Phenomenology of eccentric fixation." Am J Ophthalmol. Apr;53: 642-60.
von Ruckmann, A., Fitzke, F. W. and Bird, A. C. (1995). "Distribution of fundus autofluorescence with a scanning laser ophthalmoscope." Br J Ophthalmol 79(5): 407-12.
Wang, J., Mitchell, P., Smith, W. and Cumming, R. (1998). "Bilateral involvement by age related macular lesions in a population." Br J Ophthalmol. 82: 743-747.
Weale, R. A. (1961). "Retinal illumination and age." Trans Illuminating Eng Soc 26: 95-100.

Webb, R. H., Hughes, G. W. and Delori, F. C. (1987). "Confocal scanning laser ophthalmoscope." Applied Optics 26(8): 1492-1499.
Weiter, J. J., Wing, G. L., Trempe, C. L. and Mainster, M. A. (1984). "Visual acuity related to retinal distance from the fovea in macular disease." Ann Ophthalmol 16(2): 174-6.
Wertheim, T. (1980). "Peripheral visual acuity: Th. Wertheim." Am J Optom Physiol Opt 57(12): 915-24.
Westheimer, G. and McKee, S. P. (1980). "Stereoacuity with defocused and spatially filtered retinal images." J Opt Soc Am 70: 772-778.
Weymouth, F. W., Hines, D. C., Acres, L., Raaf, J. and Wheeler, M. (1928). "Visual acuity within the area centralis and its relation to eye movements and fixation." Am J Ophthalmol. 11(12): 947-960.
White, J. M. and Bedell, H. E. (1990). "The oculomotor reference in humans with bilateral macular disease." Invest Ophthalmol Vis Sci 31: 1149-1161.
Whittaker, S. and Cummings, R. (1990). "Foveating saccades." Vision Res. 30(9): 1363-6.
Whittaker, S. G., Budd, J. and Cummings, R. W. (1988). "Eccentric fixation with macular scotoma." Invest Ophthalmol Vis Sci 29: 268-78.
Whittaker, S. G. and Cummings, R. W. (1986). Redevelopment of fixation and scanning eye movements following the loss of foveal function. Development of order in the visual system. S. R. Hilfer and J. B. Sheffield. New York, Springer-Verlang.
Whittaker, S. G., Cummings, R. W. and Swieson, L. R. (1991). "Saccade control without a fovea." Vision Res 31(12): 2209-18.
Whittaker, S. G. and Lovie-Kitchin, J. (1993). "Visual requirements for reading." Optom Vis Sci 70(1): 54-65.
Williams, R. A., Brody, B. L., Thomas, R. G., Kaplan, R. M. and Brown, S. I. (1998). "The psychosocial impact of macular degeneration." Arch Ophthalmol 116(4): 514-20.
Wolf, E. and Gardiner, J. S. (1965). "Studies on the Scatter of Light in the Dioptric Media of the Eye as a Basis of Visual Glare." Arch Ophthalmol 74: 338-45.
Wolffsohn, J. S. and Cochrane, A. L. (1999). "The changing face of the visually impaired: the Kooyong low vision clinic's past, present, and future." Optom Vis Sci 76(11): 747-54.
Wood, J. M., Collins, M. J. and Carkeet, A. (1992). "Regional variations in binocular summation across the visual field." Ophthalmic Physiol Opt 12(1): 46-51.
Wright, K. W., Fox, B. E. and Eriksen, K. J. (1990). "PVEP evidence of true suppression in adult onset strabismus." J Pediatr Ophthalmol Strabismus 27(4): 196-201.
Zlatkova, M., Anderson, R. and Ennis, F. (2001). "Binocular summation for grating detection and resolution in foveal and peripheral vision." Vision Res. Nov;41(24): 3093-100.
Zur, D. and Ullman, S. (2003). "Filling-in of retinal scotomas." Vision Res 43(9): 971-82.

APPENDICES

Appendix 1: Consent form

BINOCULAR EYE MOVEMENTS AND ECCENTRIC FIXATION (SIDE VISION) IN AGE-RELATED MACULAR DEGENERATION

PATIENT INFORMATION BOOKLET AND CONSENT FORM

Please read this booklet carefully.
If you are unable to see the text, or if there is anything you do not understand, please ask a member of the study team for their help.

You are being invited to take part in a research study. Before you decide if you want to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with your friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Consumers for Ethics in Research (CERES) publish a leaflet entitled "Medical Research and You." This leaflet gives more information about medical research and looks at some questions you may wish to ask. A copy may be obtained from CERES, PO Box 1365, London N16 0BW.

Thank you for reading this.

What is the purpose of the study?

People with macular disease are often unable to see with the central part of the vision. However, the peripheral ("side") vision is usually good. Therefore some people with macular disease look at things with their side vision rather than by looking straight at them. Eye movements can also be disrupted. The goal of this study is to find out how people with advanced macular disease use their side vision and how they move their eyes in order to do everyday tasks like reading and recognising faces.
Such information will help us understand the disease more and help us assess better the rehabilitation techniques and low vision aids.

Why have I been chosen?

You have been chosen for this study by your doctor because you have a particular type of macular disease and your vision hasn't recently changed. Around 60 patients in your situation have been chosen for the study.

Do I have to take part?

It is up to you to decide whether or not you want to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you do decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive. If you do not wish to take part in this study you will not be at a disadvantage and will continue to receive normal clinical management.

What will happen to me if I take part?

You will be asked to come to the Institute of Ophthalmology (next to the main part of Moorfields Eye Hospital) up to 2 times over the next two years. It maybe possible to do all the tests in one visit only.

Each visit will last about two hours. During each visit, some or all of these tests will be done:

Refraction (a normal eye test)
Your ability to recognise faces will be tested using pictures on a TV monitor
Photographs of the back of your eye will be taken
A special instrument called an SLO will be used to look at the back of the eyes. You will be asked to look at different letters, shapes or words which will be shone into your eye by the machine. This is the main part of each visit.
Another instrument will look at how your eyes move while you are reading. This fits on a headband around your forehead and shines an invisible light towards your eyes.

All of these tests are safe and have been used extensively in research. None of them are painful. The tests are not difficult to do although you may be asked to keep your eyes still.

If you were not taking part in the study, only photography, pupil dilation and refraction would normally be performed when you visit the hospital; all of the other tests would not be part of normal clinical care.

It is important that you are able to set aside enough time for each visit.

You will also still have to attend the medical retina clinic to see your eye doctor in the usual way. We will try and make the clinic and research visits on the same day when possible.

What do I have to do?

Apart from visiting the Institute for each appointment, there are no restrictions on your lifestyle. You can continue to take any medicines or eyedrops as normal.

What are the possible benefits of taking part?

Taking part in the study may help you to learn how to use "side vision" more effectively. However the results of the research are also likely to be of benefit to other people who develop Macular disease in the future.

You will be given travel expenses and some money for lunch at the Friends' cafeteria at each visit.

What happens when the research study stops?

You will still be seen in the Medical Retina Clinic in the normal manner after the study stops.

What if something goes wrong?

The research does not carry any more risks than visiting the hospital in the normal way. If taking part in this research project harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms may be available to you.

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital or Institute will have your name and address removed so that you cannot be recognised from it.

Your general practitioner (GP) will be informed that you are taking part in this study, if you wish.

What will happen to the results of the research study?

The results will be published as part of a PhD thesis. They are also likely to be used at conferences or in papers (articles) in medical journals. You will not be

identifiable from any published results of the study. If you wish, copies of research papers can be given to you.

Who is organising and funding the research?

The research is being carried out between Moorfields Eye Hospital and the Institute of Ophthalmology (part of University College London). It is being supervised by Professor Gary Rubin of the Department of Visual Rehabilitation at the Institute. Professor Alan Bird and Dr Louise Culham at Moorfields are also involved in the study.

The study is being funded by the research fund of the Macular Disease Society and Research into Ageing, The Colin Kunkler Memorial Fellowship.

Who has reviewed the study?

The study has been approved by the Moorfields Research Ethics Committee.

Who can I contact for more information?

I am the person who will be carrying out most of the tests on you, and I can be contacted by telephone or by e-mail .
Contact telephone number : 0207 608 6957
e-mail: stamatina_k@hotmail.com

My name is Stamatina Kabanarou and I am an Ophthalmologist working at both Moorfields and the Institute.

Thank you for taking the time to read this booklet.

Prepared by Stamatina Kabanarou
Version 1/November 2000

CONSENT FORM

BINOCULAR EYE MOVEMENTS AND ECCENTRIC FIXATION (SIDE VISION) IN AGE-RELATED MACULAR DEGENERATION

Principal Researcher: Dr Stamatina Kabanarou

Please initial box

I confirm that I have read and understand the information sheet dated November 2000 (version 1) for the above study and have had the opportunity to ask questions. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected ☐

3. I agree to take part in the above study. ☐

_____	_____	_____
Name of patient	Date	Signature

_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature

Stamatina Kabanarou_____	_____	_____
Researcher	Date	

Appendix 2: Tables

Table 7.a Demographics of AMD patients included in the study. Description of the macular lesions observed during fundoscopy is presented for both eyes in the last two columns of the table. F=female, M=male, GA= geographic atrophy of the photoreceptors and the retinal pigment epithelium.

Subject no	*Age*	*Gender*	*Right eye*	*Left eye*
1	83	F	Disciform scar	Disciform scar
2	91	M	GA	Disciform scar
3	79	F	Disciform scar	GA
4	85	F	GA	GA
5	79	M	Disciform scar	GA
6	74	F	Disciform scar	Disciform scar
7	88	F	GA	Disciform scar
8	85	F	Disciform scar	GA
9	83	F	Disciform scar	Disciform scar
10	80	F	Disciform scar	Disciform scar
11	82	F	PED	Disciform scar
12	80	F	GA	Disciform scar
13	83	F	GA	GA
14	75	M	GA	GA
15	85	M	GA	GA
16	77	M	GA	GA
17	65	M	GA	Disciform scar
18	82	F	Disciform scar	Disciform scar
19	88	F	GA	GA
20	83	F	GA	GA
21	79	M	Disciform scar	Disciform scar
22	76	M	Disciform scar	Disciform scar
23	75	M	GA	GA
24	77	F	Disciform scar	Disciform scar
25	73	M	GA	GA
26	76	M	Disciform scar	Disciform scar
27	68	M	GA	GA
28	75	F	GA	GA
29	82	F	Disciform scar	Disciform scar
30	84	F	GA	GA

Table 7.b Results for visual acuity (in log MAR), contrast sensitivity (in log units) and MNREAD acuity (in log MAR) for both eyes for all AMD tested subjects. RE=right eye, LE=left eye, BE= both eyes, VA= ETDRS distance acuity, CS=contrast sensitivity, MNREAD= MNREAD acuity.

Subject no	*RE VA*	*LE VA*	*BE VA*	*RE CS*	*LE CS*	*BE CS*	*RE MNREAD*	*LE MNREAD*	*BE MNREAD*
1	1.00	1.00	1.00	1.35	0.95	1.05	1.13	1.51	1.03
2	0.70	1.00	0.70	1.20	0.10	1.20	0.50	1.20	0.50
3	1.00	0.90	0.80	0.85	1.35	1.35	1.20	1.00	1.00
4	0.50	1.00	0.50	1.35	0.95	1.05	0.50	0.83	0.50
5	1.10	1.00	1.00	0.40	1.00	1.00	1.50	0.90	0.90
6	1.00	0.90	1.00	1.05	1.25	1.25	1.43	1.01	0.89
7	0.40	1.30	0.40	1.20	0.00	1.20	0.40	1.50	0.40
8	1.04	0.94	0.94	0.30	0.45	0.45	1.50	1.24	1.24
9	0.90	1.00	0.90	0.35	0.75	0.90	0.86	1.11	0.83
10	1.30	1.00	1.00	0.55	1.30	1.25	1.36	1.08	1.07
11	0.30	1.30	0.30	1.05	0.75	1.05	0.50	1.24	0.50
12	0.30	1.00	0.30	1.25	1.10	1.25	0.35	1.12	0.30
13	1.30	0.30	0.30	0.15	1.35	1.35	1.50	0.40	0.40
14	0.94	1.26	0.94	0.90	0.00	0.90	1.15	1.50	1.13
15	1.00	0.40	0.40	0.05	1.20	1.20	1.42	0.44	0.42
16	1.00	0.30	0.30	1.05	1.35	1.50	0.72	0.50	0.50
17	0.30	1.00	0.30	1.25	0.95	1.25	0.80	1.50	0.80
18	1.00	1.30	1.02	1.05	0.30	0.95	1.00	1.31	1.06
19	0.80	0.70	0.70	1.05	1.15	1.30	0.93	0.87	0.76
20	1.04	0.30	0.30	0.70	1.05	1.15	1.30	0.50	0.60
21	1.30	0.56	0.52	0.30	1.05	1.05	1.34	0.52	0.52
22	1.06	0.30	0.30	0.90	1.20	1.20	1.50	0.51	0.40
23	0.98	0.96	0.94	1.05	1.05	1.20	1.08	1.04	1.01
24	1.30	0.30	0.30	0.15	1.35	1.35	1.20	0.50	0.50
25	0.64	0.84	0.70	1.20	1.20	1.35	0.87	1.02	0.91
26	0.70	0.98	0.68	1.30	0.45	1.35	0.74	1.42	0.73
27	1.00	0.72	0.76	1.05	0.60	1.05	1.21	1.10	1.34
28	0.68	0.92	0.60	1.05	0.60	1.05	0.61	1.00	0.62
29	0.80	0.98	0.80	1.05	0.75	1.20	0.99	1.26	0.89
30	1.06	1.08	1.04	0.60	0.30	0.65	1.05	1.12	1.04

Table 8.a Scotoma size (in disc areas), distance from the monocular PRL to fovea (DMFF) for the better and the worse eye, the distance between the two monocular PRLs and the angle between them.

Subject no	*Better eye scotomas size in disc areas*	*Worse eye scotomas size in disc areas*	*Better eye DMFF*	*Worse eye DMFF*	*Distance between monocular PRLs*	*Angle in degrees between monocular PRLs*
1	6	8.5	14.8	11.1	11.8	64.4
2	0.1	7.3	2.5	6.7	6.8	51.4
3	2.8	3.9	5.2	10	10	68.6
4	2.7	4.1	1.7	7.5	8.9	36.9
5	5.4		6.9			
6	6.2	13.3	13.7	19.1	6.8	13
7	0.4	9.0	1.9	8.9	10.3	82.2
8	6.1	8.7	10.5	3.0	9.9	62.1
9	3.0	10.0	0.5	12.1	11.6	20
10	8.8	9.7	11.1	11.9	6.2	29.1
11	0.1	0.5	0.9	2.4	3.1	38.9
12	0.2	3.0	0.2	9.1	9.2	28.1
13	0.09	10.0	0.7	9.7	9.5	2.6
14	6.0	6.0	6.9	5.2	3.4	3.5
15	2.1		2.7			
16	0.3	1.0	0.4	1.2	1.7	43.5
17	0.6	4.0	0.5	19.5	19.1	48.9
18	5.0	5.0	11	12.1	1.5	42.6
19	1.4	1.4	5.4	2.8	2.5	31.3
20	0.7	1.2	2.3	2.6	4.7	40.2
21	0.5	1.8	2.1	5.7	4.7	34.1
22	0.5	10.3	2.1	10.5	11.7	32.4
23	9.5	9.1	14.8	14.3	4.2	31.0
24	0.1	9.8	1.2	17.3	18.3	72.9
25	3.1	3.3	1.2	1.6	2.1	6.8
26	5.4	7.9	5.5	7.1	2.7	88.1
27	7.0	11.0	1.2	1.8	3	70.3
28	0.9	2.4	1.4	1.9	1.2	82.5
29	5.7	9.0	7.3	12.3	4.9	70.9
30	3.1	2.8	3.8	6.4	2.7	42.0

Table 8.b Distance between the two monocular PRLs in the horizontal and vertical meridian in degrees of visual angle both for patients with symmetrical scotomas (S) and asymmetrical scotomas (A).

Interocular symmetry/ asymmetry in macular scotomas	*Subject no*	*Distance in the Horizontal meridian*	*Distance in the Vertical meridian*
S	*10*	5.4	3.0
S	*11*	2.4	2.0
S	*14*	3.4	0.2
S	*16*	1.2	1.1
S	*18*	1.1	1.0
S	*19*	2.2	1.3
S	*20*	3.6	3.0
S	*23*	3.6	2.1
S	*25*	2.1	0.2
S	*30*	2.0	1.8
A	*1*	5.1	10.7
A	*2*	4.2	5.3
A	*3*	3.6	9.3
A	*4*	7.1	5.3
A	*6*	6.7	1.5
A	*7*	1.4	10.2
A	*8*	4.6	8.7
A	*9*	10.9	4.0
A	*12*	8.1	4.3
A	*13*	9.5	0.4
A	*17*	12.5	14.4
A	*21*	3.9	2.6
A	*22*	9.1	6.3
A	*24*	5.3	17.5
A	*26*	0.08	2.7
A	*27*	1.0	2.9
A	*28*	0.1	1.2
A	*29*	1.6	4.7

Table 9.a. BCEA measurements from both eyes under monocular and binocular viewing conditions for all AMD subjects.

Subject no	*Better eye monocular BCEA*	*Better eye binocular BCEA*	*Worse eye monocular BCEA*	*Worse eye binocular BCEA*
1	17546	54971	39941	82953
2	5479	8515	83079	16725
3	17195	66226	64811	53890
4	13649	13440	37620	25128
5	7943	21401	62294	32685
6	22807	41187	30761	30566
7	3126	6323	17553	21989
8	74346	145746	100716	217966
9	51723	6170	36829	33120
10	32127	8503	82457	17858
11	3099	2783	3591	1954
12	2012	1883	54141	19933
13	1726	1593	8788	3137
14	26701	30816	52072	18363
15	13582	20978	98282	100596
16	5636	7994	4437	3750
17	11355	1507	17694	2570
18	28939	37352	37278	25733
19	3911	7107	3401	2675
20	1120	850	1436	2522
21	1576	1333	16596	980
22	1500	1333	1865	747
23	487655	771499	253039	344144
24	2041	3949	57983	35682
25	18048	62195	113770	33429
26	36312	23971	14433	11033
27	23152	20997	26872	11738
28	4045	6053	34859	28561
29	6034	12325	28081	28173
30	3676	5485	20307	2139

Table 9.b. The shift of gaze position from monocular to binocular viewing conditions for the better and worse eye for all AMD subjects (in degrees of visual angle)

Subject no	*Better eye shift*	*Worse eye shift*
1	12.0	10.9
2	2.1	5.2
3	4.4	12.0
4	0.8	8.3
5	1.2	3.9
6	1.8	6.2
7	0.9	13.4
8	1.7	7.0
9	1.2	2.9
10	6.9	14
11	0.9	2.3
12	0.2	9.9
13	0.6	5.5
14	1.3	5.5
15	0.8	22.0
16	1.6	3.0
17	1.3	19.7
18	2.8	7.5
19	0.6	1.5
20	0.4	0.5
21	0.9	4.4
22	0.3	11.0
23	excluded as having multiple PRLs	
24	0.2	15.0
25	2.2	0.8
26	6.6	7.4
27	1.5	4.4
28	0.8	1.6
29	0.8	5.6
30	1.4	3.4

Table 9.c Distance from the binocular PRL to fovea (DBFF) for the better and the worse eye, the distance between the two binocular PRLs and the angle between them.

Subject no	*Better eye DMFF*	*Worse eye DMFF*	*Distance between monocular PRLs*	*Angle in degrees between monocular PRLs*
1	14.8	11.1	3.5	59
2	2.5	6.7	0.4	53
3	5.2	10.0	2.1	54
4	1.7	7.5	1.3	58
5	6.9			
6	13.7	19.1	3.0	67
7	1.9	8.9	3.6	88
8	10.5	3.0	3.7	44
9	0.5	12.1	6.5	26
10	11.1	11.9	4.5	75
11	0.9	2.4	4.1	86
12	0.2	9.1	0.6	48
13	0.7	9.7	3.6	9
14	6.9	5.2	2.1	57
15	2.7			
16	0.4	1.2	2.3	51
17	0.5	19.5	4.1	52
18	11	12.1	3.0	73
19	5.4	2.8	4.3	8.8
20	2.3	2.6	5.4	38
21	2.1	5.7	3.7	28
22	2.1	10.5	3.9	84
23				
24	1.2	17.3	3.1	84
25	1.2	1.6	3.5	60
26	5.5	7.1	3.3	67
27	1.2	1.8	3.9	24
28	1.4	1.9	1.3	54
29	7.3	12.3	1.4	1.7
30	3.8	6.4	2.8	86

Table 9.d. Distance between the two binocular PRLs in the horizontal and vertical meridian in degrees of visual angle both for patients with symmetrical scotomas (S) and asymmetrical scotomas (A).

Interocular symmetry/ asymmetry in macular scotomas	*Subject no*	*Distance in the Horizontal meridian*	*Distance in the Vertical meridian*
S	*10*	1.3	4.3
S	*11*	0.3	4.0
S	*14*	1.1	1.7
S	*16*	1.4	1.7
S	*18*	0.8	2.8
S	*19*	4.2	0.6
S	*20*	4.2	3.3
S	*25*	1.7	3.0
S	*30*	0.1	2.6
A	*1*	1.8	3.0
A	*2*	0.2	0.3
A	*3*	1.2	1.6
A	*4*	0.6	1.1
A	*6*	1.1	2.7
A	*7*	0.1	3.6
A	*8*	2.6	2.5
A	*9*	5.7	2.8
A	*12*	0.4	0.4
A	*13*	3.5	0.5
A	*17*	2.5	3.1
A	*21*	3.2	1.7
A	*22*	0.3	3.8
A	*24*	0.3	3.1
A	*26*	1.3	3.0
A	*27*	3.5	1.5
A	*28*	0.7	1.0
A	*29*	1.4	0.04

Table 10.a: Reading speed and eye movement parameters during reading with the better eye and both eyes.

bject	*Reading speed (w/m)*		*No of forward saccades*		*No of regressions*		*Fixation duration (msec)*		*Saccade size (degrees of visual angle)*		*No of saccades find next line*	
	Better eye	Both eyes	Better eye	Both eyes	Better eye	Both eyes	Better eye	Both eyes	Better eye	Both eyes	Better eye	Bot eye
	74.0	60.4	35.6	31.4	11.4	10.0	302	328	5.3	6.0	3.0	3.0
	120.0	141	25.7	35.4	10.0	14.0	264	277	3.4	2.5	2.5	2.9
	45.8	55.7	35.0	33.5	16.6	15.4	211	185	4.2	3.3	2.1	2.3
	82.5	117.0	23.7	26.7	8.6	8.8	378	255	2.6	2.3	2.2	2.6
	14.5	19.8	47.7	74.8	9.6	9.0	190	264	3.9	2.5	2.4	2.5
	68.5	64.4	28.0	24.3	8.4	5.7	323	337	1.8	2.0	2.0	1.2
	84.7	99.7	17.8	18.6	6.7	7.8	327	294	2.2	2.1	2.2	1.7
?	125.0	115.0	12.8	14.2	4.0	5.5	273	264	3.0	2.7	1.5	1.8
)	76.3	98.0	23.1	18.4	8.3	8.0	337	328	1.7	2.1	2.3	2.1
5	71.8	80.7	20.8	20.3	10.3	11.0	271	261	2.4	2.4	1.5	1.7
5	93.8	82.4	16.4	19.4	6.1	8.0	317	303	2.3	2.0	1.5	1.8
7	129	146	14.4	18.3	5.5	8.3	216	171	2.7	2.1	1.8	1.3
3	38.5	37.5	54.8	42.6	23.0	15.5	371	396	3.4	1.3	2.7	2.3
)	70.6	81.5	49.3	31.9	15.2	10.7	232	216	1.8	2.8	3.5	2.5
)	64.1	85.2	27.7	22.1	12.4	8.0	274	253	1.4	1.7	3.6	4.1
/	100.0	103.0	20.6	20.9	7.3	6.9	266	266	3.7	3.7	2.1	1.5
2	65.0	67.7	20.0	26.9	5.4	8.7	297	306	1.9	1.4	1.9	1.8
	46.1	56.7	.	.	.	.	.	.	.	.	.	.
	43.3	34.6	.	.	.	.	.	.	.	.	.	.
	74.0	60.4	.	.	.	.	.	.	.	.	.	.
3	120.0	141.0	29.0	38.0	13.2	14.7	253	204	3.0	2.0	2.5	3.3
9	45.8	55.7	42.4	44.8	13.9	16.0	243	219	2.6	2.5	3.2	4.5

Appendix 3: Presentations

Appendix 3.1

- Abstract accepted and presented as a poster at The Association for Research in Vision and Ophthalmology (ARVO) Annual Conference, Fort Lauderdale, Florida, U.S.A, May 2002.

Psychophysical mapping of the blind spot: A validation study.

S. A. Kabanarou[1], C. Bellmann[1], M.D. Crossland[1], L.E. Culham[2], E. M. Fine[3], G. S. Rubin[1]
Institute of Ophthalmology, London, UK[1], Moorfields Eye Hospital, London, UK [2], Schepens Eye Research Institute, Harvard Medical School, Boston MA[3]

Purpose: Precise mapping of the visual field in persons with age-related macular degeneration (AMD) has required a scanning laser ophthalmoscope (SLO) or other device to conrol for eye movements. SLOs are not readily available, nor practical for routine clinical use. It is possible to use the physiological blindspot as an eye position marker, and thus assure accurate fixation. To do this, one must develop a technique for mapping the blindspot. Here we compare different techniques for mapping the blindspot with monocular and binocular viewing.

Methods:10 individuals aged 20-35 years with normal vision and no known ocular pathology were tested with three different experimental techniques to map their blind spots with respect to fixation. Monocular mapping was performed with and without control of fixation using an SMI EyeLink eye tracker. The blind spot was also mapped during binocular viewing using CrystalEyes shutter glasses. Horizontal and vertical distances from centre of fixation were compared.

Results: The average horizontal distances from fixation to the centre of the blind spot were 16.6 ± 0.9 deg and 15.9 ± 1.52 deg for monocular tests with and without control of fixation, respectively, and 16.1 ± 1.7 deg for the binocular test. The differences were not statistically significant by repeated-measures ANOVA. The average vertical distances were 1.54 ± 0.8 deg, 1.81 ± 0.7 deg, and 1.98 ± 0.7 deg inferior to fixation (difference significant, $p < .05$). Posthoc comparisons revealed that the vertical distance was displaced inferiorly 28 minarc with binocular viewing compared to monocular viewing with controlled fixation ($p < .05$).

Conclusion: There was close correspondence among the different mapping techniques. Although the determined centre of the blind spot was vertically displaced during binocular viewing, the discrepancy was less than 0.5 degrees of visual angle. These techniques can now be used to compare the size and location of the physiological blind spot mapped using psychophysical measures and actual blind spot imaged with an SLO.

Appendix 3.2

- Abstract accepted at the Vision 2002, Low Vision Annual Conference, Goteborg, Sweden, July 2002

Eccentric fixation and binocular viewing in patients with advanced ARMD.

S. A. Kabanarou[1], C. Bellmann[1], M.D. Crossland[1], L.E. Culham[2], G. S. Rubin[1]
Institute of Ophthalmology, London, UK[1], Moorfields Eye Hospital, London, UK[2]

Purpose: To study eccentric fixation and explore potentials of binocular viewing in patients with advanced age-related macular degeneration (ARMD).

Methods: Patients with advanced age-related macular degeneration and central scotomas bilaterally were included in this study. EDTRS visual acuity and contrast sensitivity (Peli-Robson) were recorded. Mapping of their central scotomas and identification of their preferred retinal locus (PRL) were performed using a Rodenstock SLO (RcSLO) for each eye separately. Fixation was studied with a SMI EyeLink eye tracker and fixation stability was monitored by calculating the bivariate contour ellipse area (BCEA). Binocular viewing was explored by using the Bagolini striated glasses and the Frisby test.

Results: According to the SLO maps some patients with bilateral advanced ARMD demonstrated non-conjugate central scotomas and non-corresponding PRLs.Binocular perception seemed to be disrupted in many cases according to the binocular viewing tests results.

Conclusion: 10 patients aged 55-85years with advanced ARMD and bilateral central scotomas often develop non-corresponding PRLs, which suppress visual information from one eye and disrupt binocular viewing of the fixation target.

CR: None Support: Macular Disease Society, Colin Kunkler Fellowship

Appendix 3.3

- Abstract accepted and presented as a poster at The RiA symposium 'Meeting of minds' (UCL-2003)
  Grant number: 214

Eccentric fixation and binocular viewing in patients with advanced age-related macular degeneration.

S. A. Kabanarou[1], L.E. Culham[2], G. S. Rubin[1]
Institute of Ophthalmology, London, UK[1], Moorfields Eye Hospital, London, UK[2]

In advanced age-related macular degeneration (AMD) the patient develops a central blind spot or scotoma. In order to perceive visual information most patients with AMD use peripheral vision to perform tasks that are ordinarily done with the fovea. The peripheral part of the retina that is used as a substitute for the fovea is referred to as the preferred retinal locus (PRL). AMD often affects the two eyes differently in terms of the size and the location of the central scotomas. This incongruity may interfere with the development of the PRLs and binocular perception.

Purpose: To study PRLs and explore the potential of binocular viewing in patients with advanced AMD).

Methods: Patients with advanced AMD and central scotomas in both eyes were included in this study. Visual acuity and contrast sensitivity were recorded. Their central scotomas were mapped and preferred retinal loci (PRLs) were identified using a Rodenstock scanning laser ophthalmoscope (SLO) for each eye separately. The stability of fixation was also assessed, as it seems to be related to the efficacy of visual processing. Fixation stability was recorded by calculating a bivariate contour ellipse area encompassing 68% of the retinal area used for fixation. Binocular viewing was explored using clinical and psychophysical techniques.

Results: According to the SLO maps some patients with bilateral advanced ARMD demonstrated non-conjugate central scotomas and different PRLs under monocular versus binocular testing conditions. Binocular perception seemed to be disrupted in such cases and visual information from one eye can be suppressed.

Appendix 3.4

- Abstract accepted and presented as a poster at The Association for Research in Vision and Ophthalmology (ARVO) Annual Conference, Fort Lauderdale, Florida, U.S.A, May 2003.

Non-Foveal Fixation And Binocular Viewing In AMD

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Purpose: Eccentric viewing develops in age-related macular degeneration (AMD) when central scotomas occur in both eyes. AMD often affects the two eyes differently regarding the size and the location of the scotomas. This binocular incongruity may interfere with the development of eccentric fixation, normal eye movement co-ordination and binocular function. Therefore, the locus of eccentric fixation (preferred retinal locus or PRL) in one eye may not correspond with the PRL in the other eye, nor with the PRLs used if the subject views with both eyes. The standard techniques for determining the PRL include the fundus camera and scanning laser opthalmoscope (SLO), both of which are monocular. Video eye trackers can be used to evaluate binocular fixation, but these do not tell us directly about the retinal locus for fixation. The purpose of this study is to investigate the development of PRLs in patients with advanced bilateral AMD under monocular versus binocular viewing conditions by a combined use of an SLO and a video eye tracker.

Methods: Five patients with advanced bilateral AMD (aged 70-82 years) were included in the study. Four of them were tested with the SLO to identify their PRLs monocularly and with video presentation to identify their PRLs under binocularly viewing conditions. A previously described blind spot mapping technique (Kabanarou et al., ARVO 2002) was used to determine the location of the PRLs. In the remaining patient, PRLs were determined by mapping the blind spots under monocular versus binocular conditions using the video system only.

Results: Two of the patients used the same retinal locations to fixate under monocular and binocular conditions although visual acuities were different between the two eyes (ranged from 6/18 to 6/60) and central scotomas appeared incongruous. The remaining three patients demonstrated a shift in their PRLs in their dominant eyes when viewing binocularly. The first of them shifted his PRL horizontally and vertically by 4.1 and 3.3 deg respectively, and the second patient 2.8 deg and 3.25deg. The third patient demonstrated only a 2.9 deg shift in the horizontal plane.

Conclusions: There is evidence that when patients use non corresponding PRLs in order to fixate under monocular conditions they demonstrate a shift in their PRL when viewing binocularly. Somewhat surprisingly, this shift can occur even for the dominant eye.

Appendix 3.5

- Abstract accepted for presentation as a poster at the 'UK Multi-disciplinary Low -Vision Rehabilitation and Research Conference', Birmingham, U.K. December 2003.

Reading with central scotomas: Two eyes better than one?

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Background. Visual loss in advanced age-related macular degeneration (AMD) results from the development of a blind spot or scotoma in the central area of the field of view, the fovea. As a consequence, reading performance becomes compromised. Although AMD often affects the two eyes differently, little is known about how this incongruity affects reading ability.

Purpose. The purpose of the present study is to compare reading performance under monocular and binocular viewing conditions in patients with bilateral AMD.

Methods. 16 patients with bilateral central scotomas were recruited for this study. Assessment of their vision (distance and near visual acuity and contrast sensitivity) was performed monocularly and binocularly. Reading speed was measured using standardized texts under both viewing conditions. The ratio of binocular reading speed to monocular reading speed (for the better-seeing eye) was computed. We refer to this ratio as "binocular gain". Regression analyses were performed to determine whether clinical vision test results were predictive of binocular gain.

Results. On average, binocular reading speeds were 10% faster with binocular viewing compared to monocular viewing. However, most of the patients (62.5%) showed no significant difference in their reading speed under both viewing conditions. Three patients (18.75%) showed better reading speed with both eyes, while the other three demonstrated improved reading speed when only the better eye used. Binocular gain was not predicted by the clinical vision tests under binocular or monocular viewing conditions, or the ratio of the two.

Conclusion. In reading, binocular gain is not always apparent in AMD subjects. While most patients read equally well under binocular and monocular viewing conditions, some patients show evidence of binocular inhibition while others show binocular summation. Visual acuity or contrast sensitivity does not appear to predict binocular gain. Other variables, such as size or location of retinal scotomas may need to be taken into consideration.

Appendix 3.6

- Abstract accepted and presented as a poster at The Association for Research in Vision and Ophthalmology (ARVO) Annual Conference, Fort Lauderdale, Florida, U.S.A, May 2004.

Binocular Viewing In AMD

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Purpose: Non foveal viewing develops in age-related macular degeneration (AMD) when central scotomas occur in both eyes. AMD often affects the two eyes differently regarding the size and the location of the scotomas. Therefore, the preferred retinal locus (PRL) in one eye may not correspond with the PRL in the other eye, nor with the PRLs used if the subject views with both eyes. This binocular incongruity may interfere with the development of eccentric fixation and binocular vision. The purpose of this study is to investigate the PRLs used for binocular viewing and binocular function in patients with bilateral AMD.
Methods: Seventeen patients with bilateral AMD were included in the study. Visual acuities were recorded monocularly and binocularly with best corrected refraction. A scanning laser ophthalmoscope (SLO) was used to identify PRLs and to map retinal scotomas monocularly for both eyes. An infrared eye tracker was used to evaluate gaze position changes (and indirectly retinal locus changes) between monocular and binocular fixation. Superimposition of the eyetacker data on the SLO maps demonstrated the retinal locus used for fixation for each eye under binocularly viewing conditions. Global binocular function was tested with Bagolini striated glasses and local binocular function was tested with a computer-driven display and CrystalEyes shutter glasses.
Results: Three patients used the same PRL to fixate under monocular and binocular conditions for both eyes. Three patients demonstrated a shift in their PRLs in both eyes when viewing binocularly while the remaining eleven patients demonstrated a shift only in their worse seeing eye. We calculated the "shift distance" as the vector sum of the horizontal and vertical shift for each PRL. The range of the shift distance from monocular to binocular viewing varied from 2.88° to 17.48° of visual angle (mean 6.46 ± 3.70SD) in the latter two groups. According to SLO data, patients who used non corresponding monocular PRLs demonstrated a shift in their PRL in one or both eyes when viewing binocularly. In addition, the location of the binocular PRL in the worse seeing eye fell within the retinal scotomas in 5 patients. All patients exhibited global binocular function, but only four showed evidence of local binocular function near the PRL.
Conclusions: There is evidence that AMD patients maybe use a different PRL when viewing binocularly. Interestingly, local binocular function near the PRL seems impaired in the majority of the cases even for the subjects whose binocular PRLs fall outside macular scotomas as elicited by SLO recordings.